The BULLETIN

American Society of Hospital Pharmacists

OFFICIAL PUBLICATION OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS

DON E. FRANCKE, Editor

VOLUME 11

JANUARY-DECEMBER 1954

JAN-FEB 1954
VOLUME 11 NUMBER 1

The BULLETIN
American Society of Hospital Pharmacists

EDITOR
Don E. Francke
University Hospital
University of Michigan
Ann Arbor, Michigan

ASSOCIATE EDITOR
Gloria Niemeyer
American Pharmaceutical Association
2215 Constitution, N. W.
Washington 7, D. C.

CONTRIBUTING EDITORS
Joanne Branson
Bernard E. Conley
Leo F. Godley
Clifton Latiolais
Paul Parker
Sister Mary Etheldreda
Eddie Wolfe

ART EDITOR
Richard A. Huff

CIRCULATION
Virginia Dean

MEMBERSHIP in the American Society of Hospital Pharmacists and the American Pharmaceutical Association is open to all practicing Hospital Pharmacists. With membership is included subscriptions to THE BULLETIN of the American Society of Hospital Pharmacists and to the two *Journals* of the American Pharmaceutical Association, as well as the several services of both organizations.

ADVERTISING will be accepted, subject to editorial approval, for prescription products as well as for other items used extensively in hospitals. Inquiries should be sent to the Associate Editor of THE BULLETIN, American Pharmaceutical Association, 2215 Constitution Ave., N.W., Washington 7, D. C.

SUBSCRIPTION RATE: In the U.S. $4.50 per year (six issues), single copies 75 cents; Foreign $5 per year, single copies 85 cents. CHANGES OF ADDRESS should be directed to the Division of Hospital Pharmacy, American Pharmaceutical Association, 2215 Constitution Ave. N.W., Washington 7, D. C.

Copyright 1954
by the American Society
of Hospital Pharmacists

The American Society of Hospital Pharmacists, an affiliate of the American Pharmaceutical Association, is a national organization devoted to the profession of hospital pharmacy and dedicated to the improvement of pharmaceutical service in the interest of better patient care in hospitals.

IN THIS ISSUE

The Modern Treatment of Hypertension 23
Sibley W. Hoobler

Preparation of Ophthalmic Medication, Part I 36
John A. Scigliano and Milton W. Skolaut

Polyethylene Tubes for Eye Solutions 42
Wai-Ying Wu and Betty K. Job

The Pharmacist in Today's Hospital 43
Charles H. Letourneau

Hospital Pharmacy in Costa Rica 46
Anna May Orellana

The Formulation of a Paraldehyde Suppository 52
Harold Sheinaus and G. J. Sperandio

Public Education Program for Pharmacy Developed by American College of Apothecaries 54

A.S.H.P. Affiliates 64
As the President Sees It 66
Current Literature 55
Editorial 21
Equipment Topics 60
Letters 19
New Members 74
News Items 67
Notes and Suggestions 62
Positions 76
Therapeutic Trends 56
Timely Drugs 58

THE BULLETIN is published bimonthly at Hamilton, Illinois, by the American Society of Hospital Pharmacists in cooperation with the Division of Hospital Pharmacy of the American Pharmaceutical Association. Editorial office at 1313 East Ann Street, Ann Arbor, Michigan. Entered as second class matter July 19, 1951 at the post office at Hamilton, Illinois. CONTRIBUTIONS will be accepted if they are of general interest to those in hospital pharmacy. The editors reserve the right to revise all material submitted, if necessary. The American Society of Hospital Pharmacists and the American Pharmaceutical Association assume no responsibility for the statements and opinions advanced by contributors to THE BULLETIN. Views expressed in the editorials are those of the editor and do not necessarily represent the official position of either the American Society of Hospital Pharmacists or the American Pharmaceutical Association.

OFFICERS AND COMMITTEES 1953-54

American Society of Hospital Pharmacists

President

ALLEN V. R. BECK
Indiana University Medical Center, Indianapolis, Indiana

Vice-President

ADELA SCHNEIDER
Southern Pacific Hospital
Houston, Texas

Secretary

GLORIA NIEMEYER
2215 Constitution Ave., N.W.
Washington, D. C.

Treasurer

ANNA D. THIEL
Jackson Memorial Hospital
Miami, Florida

Executive Committee

ALLEN V. R. BECK
Indiana University Medical Center, Indianapolis, Indiana

ADELA SCHNEIDER
Southern Pacific Hospital
Houston, Texas

GLORIA NIEMEYER
2215 Constitution Ave., N.W.
Washington, D. C.

ANNA D. THIEL
Jackson Memorial Hospital
Miami, Florida

ROBERT BOGASH
Lenox Hill Hospital
111 East 76th Street
New York 21, New York

WALTER FRAZIER
Springfield City Hospital
Springfield, Ohio

J. SOLON MORDELL
U.S. Public Health Service
Washington, D. C.

GROVER C. BOWLES
Strong Memorial Hospital
Rochester, New York

GEORGE F. ARCHAMBAULT
P.H.S. Hospital Division
Washington, D. C.

Standing Committees

Committee on Membership and Organization
Adela Schneider, Chairman, Southern Pacific Hospital, Houston, Texas
Joseph E. Ball, St. Francis Hospital, Los Angeles, California
William Benka, Milwaukee County General Hospital, Milwaukee, Wis.
Johnnie Crotwell, Georgia Baptist Hospital, Atlanta, Georgia
Kenneth R. Gillmore, Indiana University Medical Center, Indianapolis.
Sister M. Rebecca Schmidt, St. Benedict's Hospital, Ogden, Utah
Sister Mary Berenice, St. Mary's Hospital, St. Louis, Missouri
Anna D. Thiel, Jackson Memorial Hospital, Miami, Florida

Committee on Minimum Standards
Walter Frazier, Chairman, Springfield City Hospital, Springfield, Ohio
Alice Appel, St. John's Hospital, Santa Monica, California
Grover Bowles, Strong Memorial Hospital, Rochester, New York
W. Arthur Purdum, The Johns Hopkins Hospital, Baltimore, Maryland
John Zugich, University Hospital, Ann Arbor, Michigan

Committee on Program and Public Relations
Robert C. Bogash, Chairman, Lenox Hill Hospital, New York, New York
Paul Bjerke, Luther Hospital, Eau Claire, Wisconsin
William McElroy, Peoples Hospital, Akron, Ohio
Lillian Price, Emory University Hospital, Emory University, Georgia
Ruth Pully, Charlotte Hungerford Hospital, Torrington, Connecticut
Evelyn Timmons, Memorial Hospital, Phoenix, Arizona
William Wissman, Methodist Hospital, Ft. Wayne, Indiana
Kenneth Wood, Indiana University Medical Center, Indianapolis, Indiana

Committee on Pharmacists in Government Service
J. Solon Mordell, Chairman, U.S. Public Health Service, Washington, D.C.
Julius Meininger, V. A. Hospital, Indianapolis, Indiana
Milton Sklaut, Clinical Center, Nat'l Institutes of Health, Bethesda, Md.

Special Committees

Committee on Special Projects
Paul Parker, Chairman, University of Chicago Clinics, Chicago, Illinois
Clifton Latiolais, University of Chicago Clinics, Chicago, Illinois
Clifton F. Lord, Creighton University, Omaha, Nebraska
Ludwig Pesa, St. Mary's Hospital, Passaic, New Jersey
Frances Rodgers, Clarkson Hospital, Omaha, Nebraska
Margaret Trevis, St. Luke's Hospital, Cleveland, Ohio

Committee on International Hospital Pharmacy Activities
Don E. Francke, Chairman, University Hospital, Ann Arbor, Michigan
Grover Bowles, Strong Memorial Hospital, Rochester, New York
Claude Busick, St. Joseph Infirmary, Stockton, California
Jacqueline Claus, U. of Houston, School of Pharm.. Houston, Texas
E. Burns Geiger, Veterans Administration, Washington, D. C.
I. Thomas Reamer, Duke University Hospital, Durham, North Carolina

Committee to Study the Role of the Pharmacist in Small Hospitals
Thomas Foster, Chairman, U.S. Public Health Service, Washington, D. C.
Jennie Banning, Saginaw General Hospital, Saginaw, Michigan
J. R. Cathcart, The Delaware Hospital, Wilmington, Delaware
J. Harold Jones, Indiana State Board of Health, Indianapolis, Indiana

Committee on Historical Records
Alex Berman, Chairman, 311 A Street, N.E., Washington, D. C.
Don E. Francke, University Hospital, Ann Arbor, Michigan
Gloria Niemeyer, 2215 Constitution Ave., N.W., Washington, D. C.
Evlyn G. Scott, St. Luke's Hospital, Cleveland, Ohio

Committee on Publications
Jane Regan, Chairman, Evangelical Deaconess Hospital, Detroit, Michigan
Don E. Francke, University Hospital, Ann Arbor, Michigan
Leo Godley, Bronson Methodist Hospital, Kalamazoo, Michigan
Paul Parker, University of Chicago Clinics, Chicago, Illinois

Planning and Advisory Committee (Past Presidents)
Grover Bowles, Chairman, Strong Memorial Hospital, Rochester, N. Y.
Walter Frazier, Springfield City Hospital, Springfield, Ohio
I. Thomas Reamer, Duke Hospital, Durham, North Carolina
Herbert L. Flack, Jefferson Medical College Hospital, Philadelphia, Pa.
W. Arthur Purdum, The Johns Hopkins Hospital, Baltimore, Maryland
John J. Zugich, University Hospital, Ann Arbor, Michigan
Hans S. Hansen, Grant Hospital, Chicago, Illinois
Don E. Francke, University Hospital, Ann Arbor, Michigan
H. A. K. Whitney, Broward General Hospital, Ft. Lauderdale, Florida

Division of Hospital Pharmacy

Members of the Policy Committee
Robert P. Fischelis, Chairman, 2215 Constitution Ave., N.W., Washington, D. C.
Glenn L. Jenkins, Purdue U. School of Pharmacy, West Lafayette, Ind.
Robert R. Cadmus, North Carolina Memorial Hosp., Chapel Hill, N.C.
Sister M. Stephanina, St. Francis Hospital, Evanston, Illinois
Allen V. R. Beck, Indiana University Medical Center, Indianapolis, Ind.
Don E. Francke, University Hospital, Ann Arbor, Michigan
W. Arthur Purdum, The Johns Hopkins Hospital, Baltimore, Maryland
Grover C. Bowles, Strong Memorial Hospital, Rochester, New York

LETTERS

From Scotland

DEAR SIRS: I thank you for your letter in regard to membership in the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS. I appreciate the honor of belonging to your organizations and would have replied sooner but have had some difficulty in getting permission to send the fifteen dollars for membership.

I hereby enclose a check for fifteen dollars and trust that this will promote a closer relationship between America and Scotland in pharmaceutical affairs.

(Miss) S. M. GRAHAM, *Chief Pharmacist*
Robroyston Hospital
Millerston, Scotland

Appreciates Formularies

DEAR SIRS: The formularies which were loaned to me from the Library at A.Ph.A. Headquarters are due back next week. I am taking the liberty of keeping them for another two-week period unless I hear from you to the contrary.

I am working on the formulary for our hospital and I am getting a lot of useful information from them. This is a fine service and I do appreciate it.

SISTER MARY DE SALES JOYCE, *Pharmacist*
St. Michael's Hospital
Texarkana, Ark.

Apply for Affiliation with ASHP

DEAR SIRS: Enclosed please find material pertinent to the completion of our organization as the Mississippi Society of Hospital Pharmacists. Those members who were not members of the national organizations have filed their applications for same. As soon as all of these are cleared and as soon as our Constitution and By-Laws are approved by the national organization, we would like to be incorporated as an affiliate and await further directions from you.

INEZ O. CAMERON, *Secretary*
Mississippi Society of Hospital Pharmacists
St. Dominics Hospital
Jackson, Miss.

DEAR SIRS: We have organized a local chapter of hospital pharmacists here in Houston and I am enclosing copies of the Constitution and By-Laws and the minutes of the meeting at which it was adopted. We wish to apply for affiliation with the ASHP. We sincerely hope that all members of the national organization will join our local society and we also hope to get a project underway early next year.

We wish to thank you for all the encouragement you and others in the national SOCIETY have given and we hope that we may be able to help organize other local chapters in the near future.

RUTH KROEGER, *Acting Secretary*
Houston Area Society of Hospital Pharmacists
Houston, Texas

From the French Hospital Pharmacists

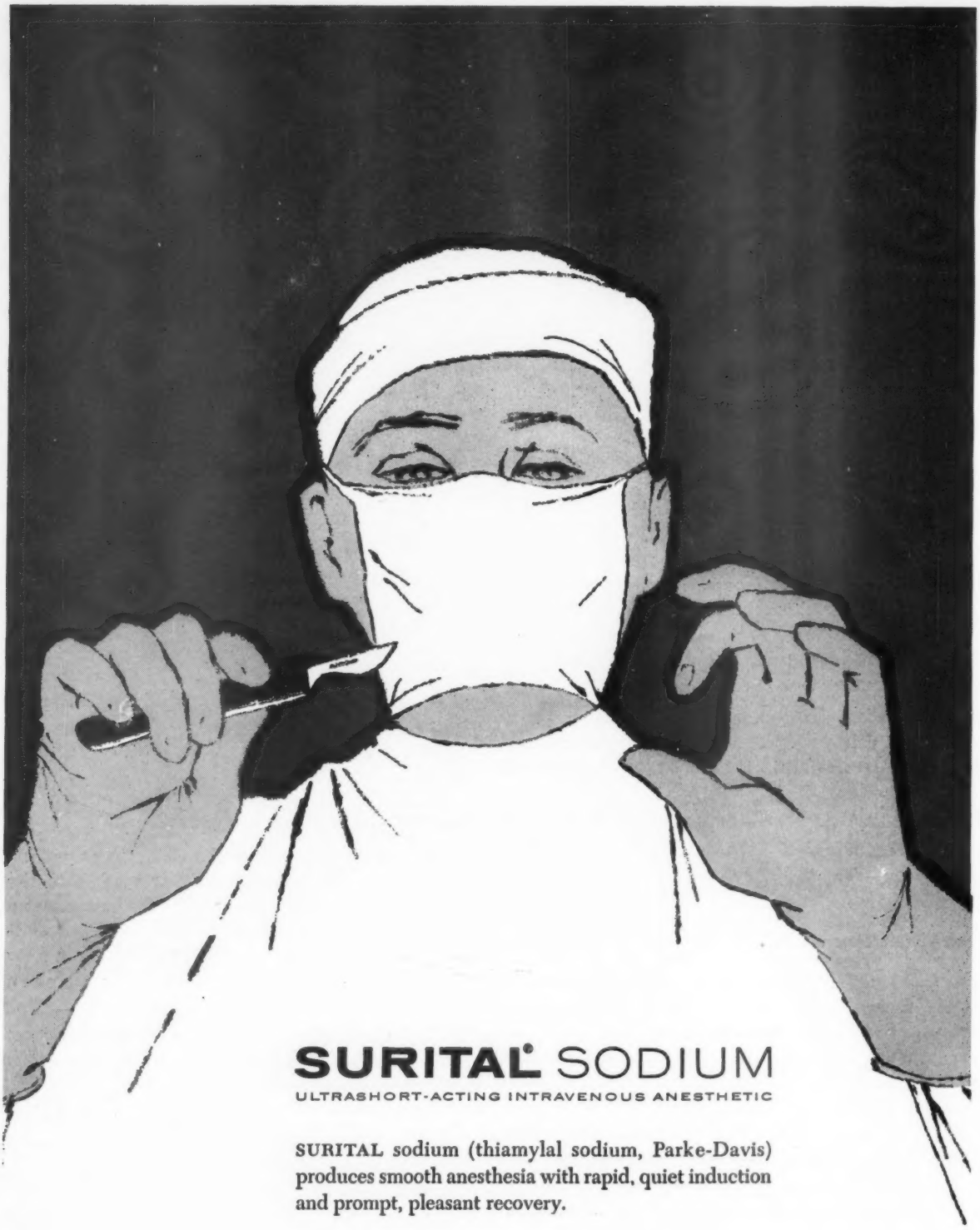
DEAR SIRS: Please excuse the delay in answering your letter of October 17. I have read it to the members of the French Hospital Federation and the French Union, and they were very appreciative. They have asked me to tell you again how happy they were to receive you and your American colleagues in Paris. . . .

Will you please be so kind as to give my most cordial greeting to the members of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

R. TRUHAUT, *President*
The French Hospital Federation
and the French Union
Paris, France

DEAR SIRS: I am a student member of the ASHP and the A.Ph.A. On graduation this May, I hope to embark on a career in hospital pharmacy. . . . I am very grateful for THE BULLETIN and the organization it represents.

ROBERT J. REYNOLDS, *student*
Southwestern State College
Weatherford, Ohio



SURITAL® SODIUM

ULTRASHORT-ACTING INTRAVENOUS ANESTHETIC

SURITAL sodium (thiamylal sodium, Parke-Davis) produces smooth anesthesia with rapid, quiet induction and prompt, pleasant recovery.

Detailed information on SURITAL sodium will be mailed you on request.

MEDICAMENTA VERA

Parke, Davis & Company

EDITORIAL

Generic Names and Substitution

by DON E. FRANCKE

It is general practice in hospitals, particularly in those with an active Pharmacy and Therapeutics Committee and a formulary, to accept basic drugs under their official or generic names rather than under the numerous brand names which are available. This practice is in conformity with the policy followed by the *Pharmacopeia of the United States* and the *National Formulary*. In stressing the advantages of generic names the Council on Pharmacy and Chemistry of the American Medical Association has included this statement in the recent edition of *New and Nonofficial Remedies*:

> The interests of the patient and physician are best served by adoption of an abbreviated scientific name for general use in prescribing, naming and identifying agents with unwieldy chemical names. The Council believes that the use of generic names in the place of trade names for prescribing tends to diminish confusion and the difficulties in learning a multiplicity of names for the same drug. . .

In spite of the general acceptance of the principle of using the generic and official names by both the professions of pharmacy and of medicine, the policy of accepting drugs under these names in hospitals often leads to accusations of substitition.

Substitution can take place only when the prescriber (or the patient) remains ignorant of the product dispensed. While hospital pharmacies, unlike retail pharmacies, may not carry numerous brands of the same basic drug, the medical staffs are well aware of this. In fact, extensive product duplication is not necessary in hospitals because of the close association and working relationship between the hospital pharmacist and the members of the medical staff. It is the lack of understanding of this relationship which most often gives rise to the charge of substitution in hospitals.

The relationship between the hospital pharmacist and the medical staff has been formalized since 1936 when the American College of Surgeons adopted the *Minimum Standard for Pharmacies in Hospitals*. This Standard provides for the formation of a Pharmacy and Therapeutics Committee and designates the pharmacist as a member and secretary of the Committee. Among the responsibilities assigned to this Committee are (1) "to develop a formulary of accepted drugs for use in the hospital", (2) "to add to and to delete from the list of drugs accepted for use in the hospital", and (3) "to prevent unnecessary duplication."

Thus it is apparent that the function of the Pharmacy and Therapeutics Committee in the individual hospital is parallel in many respects to the function of the U.S.P. Committee of Revision on a national level. The primary objective of the founders of the *Pharmacopeia* was to have each Revision supply the medical profession with "an approved list of the best known and most important medical aids available at the time of each Revision". In line with this fundamental objective, hospitals have established their committees to select the most therapeutically useful drugs and the preparations whereby these drugs may be most effectively administered. These therapeutic agents are recommended by the Pharmacy and Therapeutics Committee and are subject to approval by the medical staff as a whole and thus the formulary system becomes, in practice, one aspect of medical staff self-government.

One of the principles recommended almost universally by Pharmacy and Therapeutics Committees and accepted by medical staffs is that drugs for use in the hospitals be accepted under their generic names (even though in most instances a trade name product is dispensed). It is apparent, therefore, that a somewhat different situation exists when a prescription for a trade name drug other than the brand carried is received in a hospital pharmacy, as contrasted with that of a retail pharmacy.

The hospital pharmacist may proceed along one of two lines. Like his colleague in the retail pharmacy, he may call the physician and obtain his consent to dispense the brand available. But in addition, he may often dispense the drug under its generic name according to approval previously obtained from the medical staff. This is an orderly procedure which is accepted almost universally by members of the hospital staff.

It should be emphasized that none of those concerned with the handling of drugs in hospitals defends the substitution "with the intent to deceive" nor the product which by its size, shape, and color is produced to imitate a nationally distributed one.

The acceptance of drugs under generic names does not preclude the dispensing of trade name products, and the integrity of the pharmaceutical houses still remains the deciding factor as to the choice of brands used in hospitals. There is no basis for the charge of substitution when, as in hospitals, members of the medical and pharmaceutical professions work cooperatively together and where the policies established are known and understood by all concerned.

THE MODERN TREATMENT OF HYPERTENSION

by SIBLEY W. HOOBLER

PHYSICIANS RESPONSIBLE FOR THE MANAGEMENT of hypertensive patients are becoming aware of a quiet revolution which is occurring in this field as the result of the recent development of new and potent agents which, in combination with each other or with previously established methods, can relieve certain complications and prolong life in the more severe forms of hypertensive vascular disease. At the same time it is now generally recognized that hypertension is not "necessary" for maintainence of adequate regional blood flow but that, in forms of the disease where arteriosclerosis is not advanced, marked reductions in pressure are well tolerated.

With these changes in approach to the problem in mind, this paper proposes to deal with the older and newer treatments and the way they may be used together in the control of hypertension.

The subject may best be summarized by describing three procedures which, when successful, lower the blood pressure continuously, and three procedures in which blood pressure reduction is variable and dependent upon the dose and time

SIBLEY W. HOOBLER, M.D., is Associate Professor of Internal Medicine in charge of the Cardiovascular Unit, University Hospital, University of Michigan, Ann Arbor, Michigan.

of administration. Obviously a sustained reduction in blood pressure is to be preferred and, therefore, although these procedures are often less dramatic in short term observations they may lead to great improvement in the patient over the span of months and years.

METHODS FOR SUSTAINED REDUCTION OF BLOOD PRESSURE

Surgical Sympathectomy

The first of these measures is surgical sympathectomy, which can be shown to lower the blood pressure to a significant extent in approximately 30 percent of patients submitted to the procedure.[1] If the denervation is extended to a total sympathectomy, as many as 60 percent will report a sustained blood pressure reduction.[2] The duration of the improvement in blood pressure after the first year, at which time the above statistics have been established, is a subject of some controversy but in general it can be stated that few relapses occur over the ensuing years and that prolonged improvement reflects itself in a decreased mortality rate in all forms of hypertensive disease, an improvement in well being, and the relief of many symptoms such as headache and cardiac symptoms even in those whose blood pressure is not materially reduced. The removal of a large area of reflex sympathetic vasoconstriction also prevents the compensation which often nullifies the effects of diet and drugs and it may, therefore, make these treatments more successful. Furthermore, sympathectomy is the only treatment which does not require patient cooperation beyond the initial consent to surgery. It is extremely doubtful in my opinion that many patients now under successful drug treatment for this disease will continue to be taking these drugs successfully five to ten years hence, whereas I am certain that a great majority of patients who have undergone a successful sympathectomy will continue to have a lowered blood pressure five to ten years from now without any active cooperation on their part. This important consideration is often lost sight of by those who freely condemn sympathectomy.

Sodium Restriction

The second method of obtaining sustained blood pressure reduction, successful unfortunately in only a few cases, is dietary sodium restriction. A considerable experience with this treatment has led to the following conclusions: (a) the treatment is undoubtedly helpful whether or not it lowers the blood pressure in patients with headache, dizziness, and actual and impending congestive failure. For the latter the treatment may be life-saving regardless of its effect on the blood pressure. Symptomatic relief, particularly in the elderly, is often so impressive that patients cannot be persuaded to return to full salt intake after a trial period; (b) the treatment of asymptomatic and uncomplicated hypertensive disease is rarely successful, and to get a yield of as little as 10 to 20 percent significant improvement, one must restrict the intake to 200 mg., check urinary chloride excretions at least fortnightly, and maintain the treatment for at least three months with frequent blood pressure observations before making final judgement concerning its effects in a particular patient. If by this time reduction has not occurred the treatment may be gradually abandoned and the patient put on a general diet with selective omission of salt in food in the kitchen or on the table; (c) adjuvants such as resin, ammonium chloride, or mercurial diuretics are not worth the extra trouble in terms of the improved benefit from salt depletion; (d) an occasional individual will develop the salt depletion syndrome with weakness, nausea, and rising NPN, particularly when his renal function is borderline.

TABLE I. *Rauwolfia serpentina* AND RESERPINE

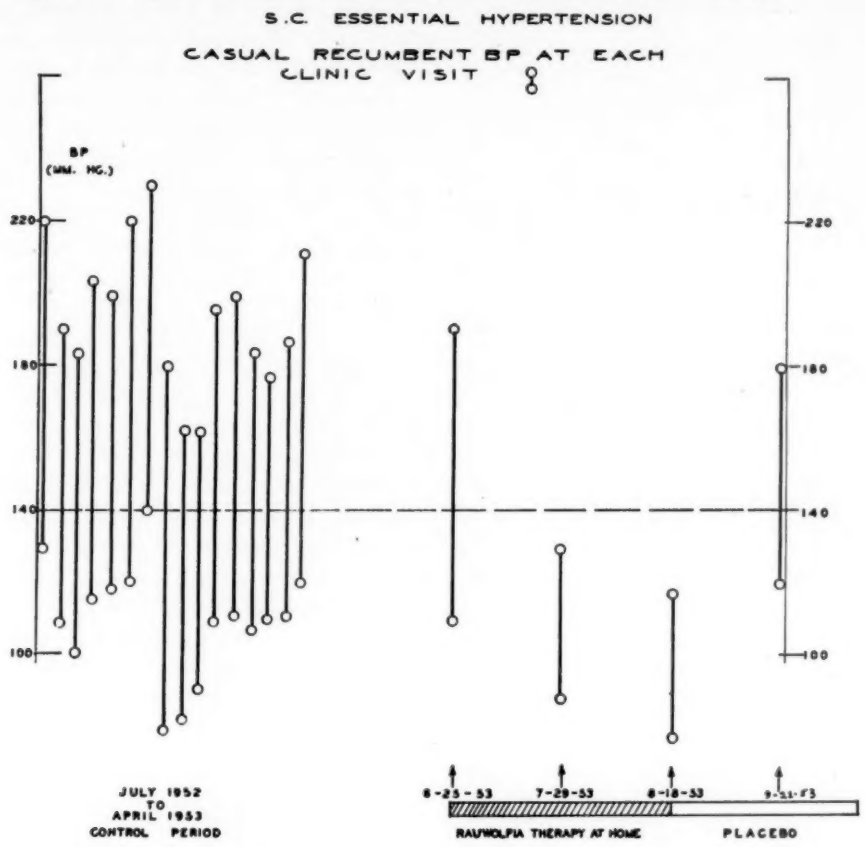
DRUG AND ORAL DOSE	*Rauwolfia serpentina* (Raudixin - Squibb) 50 to 100 mg. two to three times a day. Reserpine (Serpasil - Ciba) 0.25 to 0.5 mg. two to three times daily.
MODE OF ACTION	? hypothalamic with central sympathetic inhibition, parasympathetic stimulation.
TREATMENT OBJECTIVE	Moderate sustained blood pressure reduction.
SIDE EFFECTS	Useful: decrease in pulse rate and anxiety, increase in appetite and in weight, increased bowel movements. Unpleasant: fatigue and nasal stuffiness. Serious: none
PRECAUTIONS	None.
GENERAL CONTRAINDICATIONS	Fatigue, obesity.

USE OF DRUGS

Rauwolfia Alkaloids

The third method of treatment is the selective use of drugs. The administration of rauwolfia alkaloids, when successful, provides a sustained reduction in blood pressure. In Table I the chief pharmacologic actions are described and in Figure I the use of the compound in a typical case of hypertension is demonstrated. Reductions in blood pressure are always moderate in magnitude,

Figure I. Effect of Rauwolfia Therapy on Casual Blood Pressure



Gradual sustained reduction in blood pressure over a two month period of Rauwolfia therapy with return of hypertension when placebo substituted. Casual blood pressures are recorded on admission to Hypertension Clinic, last dose of drug having been taken the night before.

but will occur in about 20 to 30 percent of individuals, are not correlated with other evidence of drug effectiveness, but come at a later time interval from two weeks to three months following institution of treatment. The reduction in blood pressure is very gradual, and once established does not fluctuate with each dose. A return to previous hypertensive levels occurs very gradually over a week or more while the other side effects cease in a few days. The exact dosage for effective action is likewise unpredictable. In the absence of knowledge of the minimal effective dose, we tend to treat with larger than the usual amounts, giving about the dose which the patient can tolerate without major unpleasant side effects and then reducing the dosage as far as possible when a definite reduction in blood pressure has been secured. The pure rauwolfia alkaloid, reserpine, seems responsible for most of the clinical effects, and there is probably no justification in the use of cruder preparations with inert ingredients unless they are made substantially less expensive by the manufacturers. The drug may be given intravenously and again exhibits a peculiar delay in its effectiveness and remarkable safety. The slow intravenous infusion of 2 to 3 mg. of reserpine is said to lead to a long period of sedation without interference with respiration, and a decline in pulse rate and blood pressure, which may last for several days. This technique may find usefulness in the occasional treatment of the severely agitated hypertensive patient. Administration of the oral forms of rauwolfia alkaloids are indicated in the treatment of early hypertensive patients with anxiety and vasomotor storms, some of whom will be benefited, and others not. The drug may also be tried in the elderly hypertensive, again with marked individual variation in the therapeutic effect. It can be used as an adjunct to other forms of drug treatment of hypertension and this will be discussed below. Full advantage should be taken of certain of the beneficial side effects. The improvement of appetite and gain in weight is an extremely interesting feature of the drug action but may contraindicate its use in the obese hypertensive patient.

TABLE II. HYDRALAZINE HYDROCHLORIDE

DRUG AND ORAL DOSE	Hydralazine Hydrochloride (Apresoline Hydrochloride - Ciba) 10 to 150 mg. three to four times a day.
MODE OF ACTION	Direct vasodilator.
TREATMENT OBJECTIVE	Moderate diurnal blood pressure reduction in some cases.
SIDE EFFECTS	Useful: circulatory stimulation; increased renal blood flow. Unpleasant: headache, gastrointestinal symptoms, tachycardia, palpitation. Serious: drug fever, arthritis resembling lupus erythematosus.
PRECAUTIONS	Avoid in drug-sensitive patients.
GENERAL CONTRAINDICATIONS	Angina, ? congestive heart failure.

Effective but Intermittent Blood Pressure Reduction

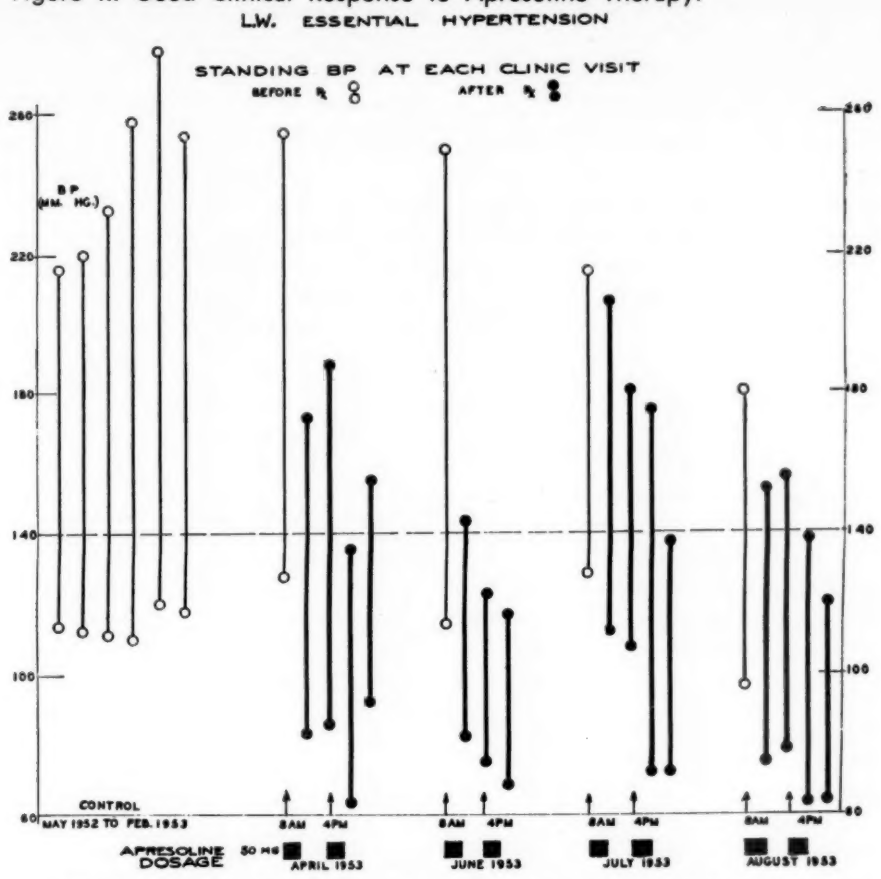
From the foregoing, it can be seen that sustained moderate reduction in blood pressure can be achieved in a fair percentage of "benign" hypertensive patients by sympathectomy, diet-therapy and rauwolfia drugs. Unfortunately these treatments are least likely to lower the blood pressure in the most severely hypertensive. In these cases it is necessary to use more active depressor drugs with more transient action and more frequent side effects.

Hydralazine (Apresoline)

The first agent of this group, hydralazine (Apresoline — Ciba) is summarized in Table II and its clinical use exemplified in Figure II. The graph illustrates the fact that the blood pressure reductions were most marked in the early afternoon and toward evening, with a rise in blood pressure by the following morning, thus illustrating the fact that this agent is rapidly excreted and has to be given four to five times a day to achieve blood pressure reduction. The apparent progressive decline in initial morning blood pressure on prolonged therapy is probably not the result of Apresoline or at least is not usually seen. In a number of patients treated with this drug alone acute daily reductions of lesser magnitude than this were demonstrated; there was no tendency for the "basal" blood pressure to fall; and even a tolerance to the initially effective dose was noted over a three months' treatment period.[3] However, this drug is unique in increasing cardiac output and circulation through the kidney and splanchnic areas, thus superimposing a physiologic and symptomatic state not unlike hyperthyroidism upon the hypertensive individual. This leads to abandoning medication in approximately 30 percent of cases owing to the frequency of excitatory side effects. Another 30 percent while tolerating maximal doses, will not show significant reductions in blood pressure. The remainder at a varying dosage level will have satisfactory hypotensive effects although the development of tolerance and occasional side effects may interfere with prolonged management with this agent alone. When Apresoline is combined with hexamethonium many of the cardiac excitatory side effects such as palpitation and tachycardia are abolished and the depressor effects are magnified since the buffering effect of the sympathetic nervous system on the vasodilator action of the drug is abolished. Consequently these two appear to be a rational combination of therapeutic agents. A serious drawback of uncertain significance at this time is the development of an arthritis-like syndrome with many features of lupus erythematosus after prolonged treatment with Apresoline.[4] When the drug is given in large doses (400 to 600 mg. daily) as many as 8 percent will develop this complication in a year or more of treatment. For this reason it is the author's present opinion that the drug should be limited to small doses, not exceeding 75 mg. four to five times daily, when used alone or in combination in the treatment of hypertension, and that other methods of treatment should be applied first, when possible.

Theoretically Apresoline may have unique benefit in patients with marked renal impairment because of the increase in renal blood flow so produced. However, glomerular-filtration rate is not increased and thus the removal of excretory products is not hastened in these individuals. Any benefit to be derived from renal vasodilatation must reside in the improvement of blood supply to the renal tubular cells. This is largely theoretical and to my knowledge improvement in excretory function has never been clearly attributable to Apresoline alone. Investigators at the Cleveland Clinic feel that this drug is particularly helpful for the cerebral complications of hypertension, and since it is an active stimulant of the circulation, one might hope that cerebral blood flow would also be benefited. Their clinical observations tend to bear this view out but, unfortunately for the theory, specific measurements of the cerebral blood flow do not show increases when Apresoline is administered.[5] Furthermore the author has seen three cases of cerebral thrombosis occur while the patients were an Apresoline therapy. While these individuals were admittedly

Figure II. Good Clinical Response to Apresoline Therapy.



Effect of Apresoline on blood pressure over a four month period. Drug administered during a clinic day as indicated, as well as at home in same dosage in intervals between visits. The apparent progressive decline in initial blood pressure is unusual, not having been observed in other cases with equal diurnal responses to the medication.

bad risk patients and the drug is not thought to have accelerated thrombosis, these scattered observations tend to deny its validity in the treatment or prevention of cerebral thrombosis. When Apresoline is administered without concomitant hexamethonium, stimulation of cardiac output and pulse rate is such as to induce angina. Therefore it is probably contraindicated in this condition.

Protoveratrine

The veratum alkaloids have long interested investigators in hypertensive disease. Their dramatic hypotensive effects along with the preservation of circulatory homeostasis, have recommended them, but the close association of nausea and vomiting have led to poor patient acceptability. The action of these compounds is summarized in Table III. With the development of protoveratrine, a single purified alkaloid from *veratrum album,* it was hoped that accurate dosage, elimination of emetically active contaminants, and better standardization might demonstrate its therapeutic superiority over cruder products from *veratum viride*. These hopes have proved to be only in part correct. It was found in our Hypertension Clinic that it was impossible to maintain hypertensive individuals on a sufficiently large maintenance dose of protoveratrine to lower the blood pressure without producing emesis. On the other hand, intravenous or acute oral administration of a single dose was rarely associated with vomiting. It was therefore postulated that hypotensive effects preceded emetic ones and that if saturation of the body could be prevented by repeated single large doses with adequate intervals for excretion, a worthwhile treatment plan could be devised for the ambulatory management of hypertensive patients. This proved possible in 50 to 70 percent of individuals, but at the expense of limiting the period of effective hypotension to 4 to 6 hours out of each 24. While this was by no means optimal, it did lead to substantial impro-

Table III. Protoveratrine A and B Maleates

Drug and Oral Dose

Protoveratrine A and B Maleates (Provell Maleate - Lilly) 0.75 to 1.5 mg. after breakfast and 0.25 mg. 2 hours later. Similar dosage may be repeated after supper if tolerated.

Mode of Action

Afferent stimulation vasomotor centers, with ? sympathetic inhibition and parasympathetic stimulation.

Treatment Objective

Recumbent or standing blood pressure reduction 4 to 6 hours daily.

Side Effects

Useful: decreased pulse and increased cardiac efficiency.
Unpleasant: nausea, vomiting, extreme hypotension.
Serious: heart block.

Precautions

Omit during acute digitalization.
Intravenous atropine sulfate for heart block.

General Contraindications

Cerebral arteriosclerosis.

vement in symptoms and in signs of hypertensive disease at the cost of very few side effects.[6] However, to achieve these results it was necessary to pay constant careful attention to such details as giving the drug immediately after breakfast and a supplementary dose two hours later and advising the patient not to take food for two hours after that. It was also found advisable to test patients repeatedly to detect slight shifts in tolerance. No antiemetic agent was found capable of suppressing the vomiting stimulus when too great absorption of the oral dose occurred. Chlorpromazine given parenterally was of some therapeutic value but proved not to be an effective prophylactic against protoveratrine nausea.

At first this agent seemed the best one available for the management of severe hypertensive disease, although its shortcomings were apparent. At present we feel that hexamethonium is generally more useful in severe hypertension, but favor protoveratrine when renal failure is advanced since it does not have cumulative effects in the uremic hypertensive. While it will not change the fatal outcome of severe azotemia it is often helpful in relieving cardiac and cerebral vascular symptoms associated with this condition. It also has a definite field of usefulness in the management of eclampsia and toxemia of pregnancy, particularly since hexamethonium may be injurious to the fetus.[7] Finally its effects on the heart rate and perhaps on the strength of ventricular contraction recommend it in hypertensive heart disease particularly associated with renal failure where control of hexamethonium therapy may be very difficult.

Observations on the Use of Ganglionic Blocking Agents

At the present time long-acting ganglionic blocking agents appear to be the most effective long term treatment for hypertensive disease. The use of these agents predisposes a considerable knowledge of their pharmacologic effects and also includes a considerable area of controversy. Table IV illustrates some of these.

There are four major considerations that should be always kept in mind by the physician who prescribes these compounds. First, they produce marked orthostatic hypotension and the patient must be protected against the consequences of occasional syncopal attacks as in crowds, streetcars and in close quarters where it is not possible to quickly resume the recumbent position. Fortunately orthostatic syncope is rare in the sitting position although in patients unusually sensitive to gravity effects, driving a car may be dangerous. Secondly, blockade of the parasympathetics may lead to ileus, which, if not detected in time, may be fatal. The forewarning of ileus is always constipation and decreased bowel activity, usually with distention. If the patient is instructed to take no more drug when this first occurs, and if he is accustomed to having a daily bowel movement, this complication can be prevented. For this reason we like to prescribe a saline laxative daily and insist on a daily bowel movement before treatment is continued. This is particularly important when the drug is administered orally since absorption appears to be a function of the time of contact with the intestinal mucosa. The average individual absorbs only 5 percent of these compounds but if the fecal stream is delayed by constipation, he may absorb twice as much leading to severe hypotension and further aggravation of the constipated state. It is for this reason that ileus can occur abruptly and unexpectedly on oral therapy, and this is why we allow no compromise with the rule of discontinuing medication after a 24 hour period without a bowel movement. Thirdly, the drug is not metabolized in the body but is excreted in the kidney at the same rate as other substances which are filtered through the glomeruli. If this function is seriously impaired as in malignant hypertension, very small doses will be retained in the body and will have an exaggerated effect. If the blood pressure is lowered excessively, glomerular filtration will all but cease and the drug cannot be excreted. In this emergency an infusion of nor-epinephrine or other vasocon-

TABLE IV. HEXAMETHONIUM CHLORIDE AND PENTAMETHYLENE PYRROLIDINIUM BITARTRATE

DRUG AND ORAL DOSE

Hexamethonium Chloride (Esomid Chloride - Ciba; Hexameton Chloride - Burroughs Wellcome; Methium Chloride - Warner-Chilcott). 125 to 750 mg. (orally) three times a day after meals and at bedtime.

Pentamethylene Pyrrolidinium Bitartrate (Ansolysen-Wyeth) 10 to 200 mg. three to four times a day.

MODE OF ACTION

Ganglionic blockade of both sympathetics and parasympathetics.

TREATMENT OBJECTIVE

Marked orthostatic and some recumbent blood pressure reduction.

SIDE EFFECTS

Useful: decreased tendency to vomiting.

Unpleasant: weakness, cycloplegia, dry mouth, constipation, occasional dizzy spells, impotence.

Serious: ileus, bladder paralysis, progressive azotemia.

PRECAUTIONS

Daily saline laxative; omit if constipation more than 24 hours.

GENERAL CONTRAINDICATIONS

Prostatic hypertrophy; cerebral arteriosclerosis; azotemia.

strictor agents may be life saving by raising the pressure, permitting glomerular filtration and thus gradually removing the drug from the circulation. A fourth aspect of treatment with this agent which is very puzzling is the wide difference in initial sensitivity and the later development of a variable degree of tolerance to the hypotensive effects of the drug. Sensitivity is increased in malignant hypertension, and in conditions associated with increased intracranial pressure such as encephalopathy or cerebral hemorrhage. Initially the recumbent as well as the standing blood pressure is reduced but usually the recumbent blood pressure rises toward pretreatment levels while orthostasis persists. After several weeks very high dosage may be necessary even to maintain orthostatic hypotension.

After several months of treatment, during which the dose must be constantly changed, a steady state is finally reached, which may be either: (1) insufficient reduction in recumbent or orthostatic blood pressure to justify further treatment; (2) good reductions in standing blood pressure but little change in recumbent blood pressure, a state of affairs usually seen in sympathectomized patients, and illustrated in Figure III; (3) reductions in both recumbent and standing blood pressures. In the first instance if the need for treatment is sufficiently urgent, Apresoline may be added to the regimen at this point if one is willing to accept the possibility of the long term complications mentioned above. Perhaps a preferable adjunctive treatment, at least initially, is the addition of rauwolfia to the program. The depressor effects of this drug are at least additive and its gentle stimulation of bowel activity, and sedative effect may make the ganglionic blocking agent more acceptable as well as promoting its effectiveness. In cases where the orthostatic effect is prominent but the recumbent pressures are very high at night, the administration of a single dose of protoveratrine may be given at bedtime in order to maintain blood pressure reduction in recumbency.

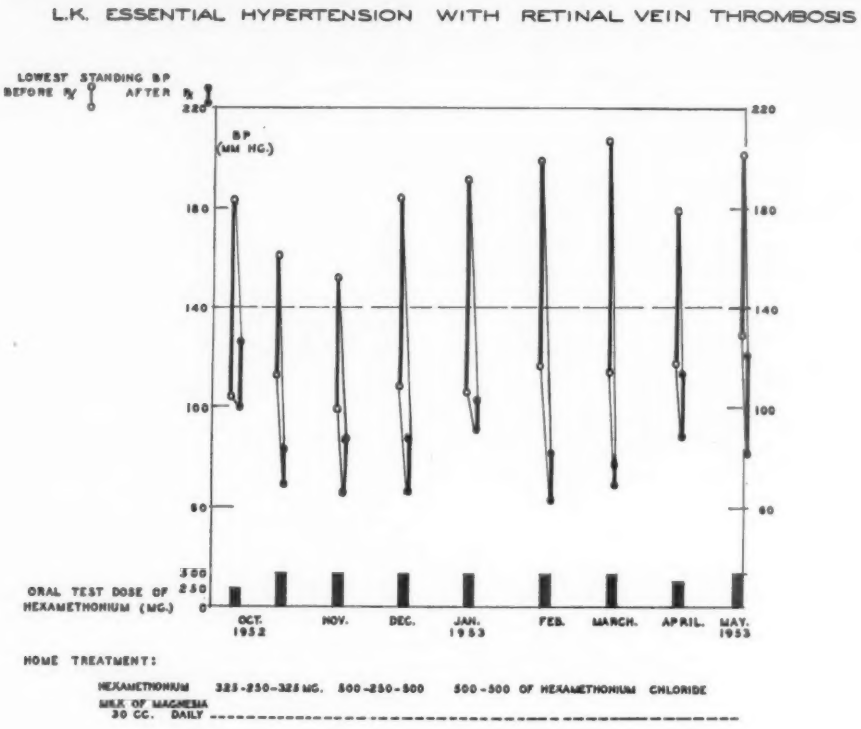
Pentamethylene Pyrrolidinium Bitartrate

As a result of an extensive screening program by British chemists at May & Baker, a new ganglionic blocking agent pentamethylene pyrrolidinium bitartrate (M & B 2050A) has been synthesized. In clinical tests this has shown less parasympathetic blocking effect, five times the potency of hexamethonium and one and a half to two times the duration of action.[8] Reports in the British literature and experience in this Laboratory indicate that it is extremely acceptable and will probably supplant hexamethonium entirely. It is hoped that, because of its increased potency and less effect on the bowel, more patients can be controlled on this drug, at least so far as their orthostatic blood pressure is concerned. In this country pentamethylene pyrrolidinium bitartrate is being distributed, at present only for investigational use, by Wyeth Laboratories under the name of Ansolysen.

Oral vs Parenteral

In the chronic use of ganglionic blocking agents some matters of controversy persist. Some investigators feel that these compounds should be given only parenterally because of the irregularity of their absorption when given orally. Apart from questions of practicality for prolonged treatment, it is my opinion that the duration of effective reduction of blood pressure is reduced and dips in blood pressure are accentuated, so that in order to obtain a significant reduction for more than two to three hours the patient must lie down for half an hour or more after the injection and must give himself at least three to four injections daily to achieve an effect comparable to good absorption of the oral drug given as frequently. Some investigators advise oral administration be-

Figure III. Effect of Oral Hexamethonium Therapy.



Graph illustrating a predominant orthostatic hypotensive response to hexamethonium. Initial standing blood pressure at 9 A.M. on each clinic day was little affected by drug but usually the test dose given at about 9:30 A.M. had reduced the standing blood pressure by 1 P.M. to the levels indicated with only moderate concomitant reduction in recumbent blood pressure. Patient took dose indicated daily at home, suffered no disability from treatment whatsoever, and had gratifying improvement of vision.

fore meals to produce a greater reliability of absorption. On the contrary, it is my opinion that when given just after meals hexamethonium has a more predictable action and is less likely to be suddenly absorbed and thus may give a smoother action throughout the day. Of all factors, the speed of the fecal stream is probably the most important. Consequently in a patient having a regular stimulus and a regular bowel movement daily, the variability in absorption does not seem to be a major difficulty. It is probable that the long acting product mentioned above will obviate some of these difficulties as it is slower in onset of action as well as offset when administered orally. Another point of controversy concerns the therapeutic objective. Smirk, who has had the longest experience with these compounds, seeks to maintain a near normal sitting blood pressure.[9] In most individuals this will yield a moderate reduction in the recumbent blood pressure at the time of maximum drug effect and a reduction in the motionless standing blood pressure to barely above the point of dizziness. Thus, he finds a necessary point of reduction if treatment is going to produce significant results on the usual ambient blood pressure. Smirk points out further, that if just prior to the administration of the next dose the patient makes a test of motionless standing for a minute or more, and is not dizzy, it is probable that he has not absorbed too much of the drug for safety. On the other hand if dizziness occurs at this late time interval after the preceding dose, the subsequent dose should be reduced by half. This maneuver, which is simple and practical, will prevent overdosage without requiring the patient to monitor his blood pressure constantly as in some therapeutic programs that have been recommended. On the other hand, of course, it will not tell him if his dosage program is ineffective. This can be done only by returning to the doctor's office for blood pressure determinations throughout the day or by having

a cuff in the home. Which of these two procedures to adopt is at the moment controversial. We favor reducing the blood pressure so gradually in the average case that we like to have the opportunity to follow the patient in the office and increase the dosage as indicated. On the other hand, it is undeniable that office blood pressures and home blood pressures are not comparable; in severe hypertensive disease "escape" from drug effects may occur before the next visit and lead to the recurrence of complications. While it seems possible to protect the patient against hypotension by Smirk's maneuver, and to protect him against paralytic ileus by strict insistence on laxatives and by omitting treatment if bowel movements are delayed, it does not seem possible to control the upper limit of his blood pressure without teaching him to measure it himself. It would seem that this aspect of treatment needs individualization, depending upon the severity of the disease and the intelligence and attitude of the patient.

Schroeder is not satisfied with achieving reductions in the orthostatic blood pressure alone. In his experience recumbent blood pressure is not altered in well over 50 percent of patients on hexamethonium therapy alone, and orthostatic effects are insufficient. He postulates the secretion of a humoral substance from the kidney to account for the tolerance phenomenon, and believes that Apresoline specifically antagonizes this humoral agent. He, therefore, advises that both drugs should be given together in whatever dosage is necessary to produce complete normalization of the blood pressure day and night. This is indeed a heroic and difficult objective and often requires oral administration of as much as one gram of hexamethonium and 150 mg. of Apresoline every four hours, the magnitude of the hexamethonium dose being varied up or down, depending upon the blood pressure just before it is to be taken. This rigid regime appears to be effective but at the cost perhaps of making therapeutic addicts and inviting the ultimate development of the lupus erythematosus syndrome on long term treatment. While we do not adopt this extreme form of therapy in the Hypertension Clinic of the University Hospital, believing that for most hypertensives a lesser reduction of blood pressure will accomplish almost as good results, it cannot be denied that Schroeder's statistics are impressive.

Specific Methods of Treatment

It will be seen that the exact method of treatment of severe hypertension with ganglionic blocking agents is still a matter of controversy. In Table V we present the program which is currently followed at the University of Michigan for oral treatment with these agents. Most patients are started in the hospital, where the increases can be made more rapidly and where overdosages can be corrected by the nursing staff by following the appropriate "stop" orders. The build up

TABLE V. ORAL DOSAGE PROGRAM FOR CHRONIC TREATMENT OF HYPERTENSION

DRUG	FREQUENCY	TOTAL DAILY DOSE			
		INITIAL	DAILY INCREASE	MAXIMUM	DECREASE OR OMIT
Hexamethonium Chloride	3 x daily after meals and at bedtime.*	500 mg.	250—500 mg. daily (until standing blood pressure falls to 140 systolic just before the next dose.)	3 Gm.**	If standing blood pressure is less than 120, give one-half dose; or omit if less than 100, or no bowel movement in 24 hours.****
Pentamethylene pyrrolidinium bitartrate***	3 x daily approximately 7 hours apart.	60 mg.***	30 mg. daily	800 mg. (?)	Use same precautions as with hexamethonium chloride

* Some advocate administration before meals.

** This maximum dose is controversial and many physicians are using larger doses. However, complications of ileus are more likely to occur and we prefer adding Rauwolfia alkaloids or hydralazine (Apresoline) to the regimen at this point.

*** To convert patient from hexamethonium to pentamethylene pyrrolidinium bitartrate, approximately one-fifth as much of the latter drug is given either orally or parenterally.

**** Treatment must *never* be stopped abruptly for longer than necessary to secure adequate bowel activity or a restoration of blood pressure. Sudden cessation of treatment may lead to serious and fatal hypertensive "rebound". If treatment has been stopped for more than a few days sensitivity will return and the drug dose will have to be reduced to avoid serious hypotension, and then increased gradually as tolerance returns.

program may be accomplished more gradually in the Outpatient Department, but each increment should be taken with the doctor's observation in the Hypertension Clinic. If the patient is sufficiently intelligent, he may record his own blood pressures and guide his dosage by the program outined. Where treatment with hexamethonium is likely to be difficult owing to poor renal function, the institution of treatment with parenteral medication may be advisable since more accurate control can be established. In these circumstances we start with 5 mg. of hexamethonium subcutaneously every four hours, increasing dosage by 5 to 10 mg. increments daily until the effective level is reached. Caution in building up the dosage is mandatory since patients with renal failure may convert with startling rapidity from individuals with apparently inadequate ganglionic blockade to patients with paralytic ileus and hypotension. Even if the bowels are kept open, too rapid a reduction in blood pressure or too marked a reduction may lead to azotemia. We therefore advise determination of serum creatinine values as an index to therapy and we try to depress the blood pressure much more gradually, perhaps by decrements of 20 to 30 mm. every three to four days, stopping further reduction if the creatinine begins to rise. Under these circumstances it is probably wise to add Apresoline to the regime. It may be added on the third or fourth day of therapy when ganglionic blockade is sufficient to eliminate its side effects but should be given in small doses first as these patients are sensitive to this drug as well. A suggested routine would be 25 mg. four times the first day, increasing by 100 mg. daily until a total daily dose of 400 to 600 mg. is being administered.

Drug Combinations

From the foregoing discussion, it is apparent that drug therapy of hypertension cannot be planned intelligently if the physician uses drug mixtures, compounded in one tablet. It is unfortunate that many physicians demand these combinations and that drug houses are supplying them. In my opinion treatment for hypertension should be left as simple as possible. One drug only should be started and explored to maximum effectiveness. If the reduction is not satisfactory or the side effects disturbing, another drug may then be added separately. While it may not make much difference where altering of the hexamethonium or protoveratrine or Apresoline dosage requires changing the concomitantly administered rauwolfia; it is poor treatment and poor pharmacy to encourage this practice. If hexamethonium and rauwolfia are to be given together, for example, one wants to use the least amount of each which will be effective. This cannot be done with combined tablets. The situation with respect to the veratrum alkaloids is even more critical. There is no reason why some other medication should be given in twice or half the proper dosage in order to save the administration of a second pill to the patient!

Treatment of Hypertensive Emergencies

The technic of emergency administration of hypotensive drugs should also be mentioned briefly. It is probably safe to administer hexamethonium intravenously very cautiously when the patient is comatose and one has reason to believe that blood pressure reduction may be beneficial. Since such individuals, particularly after the first dose, are extremely sensitive, the medication must be given very cautiously at the rate of 0.5 to 1 mg. per minute by intravenous drip with the patient in the sitting posture if possible, and with the drip to be stopped at the moment of reduction in the systolic blood pressure. If the patient has a uremic odor to the breath, even the very smallest dose of hexamethonium may produce serious collapse and this treatment should, I believe, be avoided in favor of the use of a more transient and reversible depressor agent such as protoveratrine. The latter drug may be given in a dosage of 1.4 micrograms per kilogram in a single dose intravenously followed in 8 to 10 minutes by an additional dose of 0.02 to 0.06 mcg.

Another useful agent with which we have had a little experience is Arfonad[10] which is given in a dosage of 1 to 3 mg. intravenously per minute. Chemically Arfonad is d-3,4-(1′3′-dibenzyl-2′-ketoimidazolido 1,2 trimethylene thiophanium d-camphor sulfonate. It is a direct vasodilator as well as having a very brief ganglionic blocking action. It is still available only for investigation. For this reason and because it has no effect when given orally in chronic treatment, it has not been discussed previously in this article.

These agents do not depend on the kidney entirely for excretion and are therefore particularly useful in uremia and in circumstances where careful control of the blood pressure reduction is necessary. Arfonad has the added advantage that being rapidly metabolized, its effect will wear off quickly, and if lowering of blood pressure has an unexpectedly adverse effect, it will not be as sustained as with hexamethonium. Protoveratrine would probably be preferable for most emergencies of this sort, except that the delay in effect makes

the calculation of an accurate dosage difficult. It is possible to administer protoveratrine by a slow intravenous drip and obtain satisfactory blood pressure control. Here, too, the rate of administration is critical and decisions must be made for slowing or increasing the drip five minutes or so in advance of the event. Meilman[11] has studied this technic in detail and describes it effectively. Unfortunately, in our experience prolonged blood pressure reduction by this means is usually associated with emesis. This may be particularly undesirable in an unconscious patient. Protoveratrine has the advantage of slowing the pulse and improving cardiac action. Arfonad on the other hand has a cardio-accelerator property. It does carry the great advantage of having an almost immediate effect on the blood pressure and almost as sharp an offset of action when the drip is slowed down or discontinued.

Treatment of Specific Complications

In the closing section of this paper an attempt will be made to summarize the specific clinical situations in which surgical, dietary, or drug treatment is helpful. This rough guide derives largely from our personal experience in the Hypertension Clinic and is obviously subject to change as experience proceeds.

General Considerations

We must never forget that we are treating patients with hypertension rather than the blood pressure itself despite the emphasis which is of necessity laid on the latter. The personality of the patient must affect our thinking in many ways. The irresponsible or inaccessible patient will do well with a sympathectomy if the clinical situation warrants it. The tense and nervous early hypertensive is often more relaxed and less subject to vasomotor storms after sympathectomy, even though these procedures have little measurable effect on the blood pressure. One must steer a narrow road between the extremes of too much emphasis on the blood pressures and completely disregarding its warning sign. Many symptoms are abolished by sympathectomy but some are made worse, notably fatigue, weakness, and angina. Raynaud's disease and peptic ulcers are likely to be worsened by splanchnicectomy. The easily excitable patient, or the patient who gives a history of drug reactions, will not do well on Apresoline. The obese will gain weight on *Rauwolfia serpentina* and the fatigued will become worse. On the other hand, patients with tachycardia and palpitation will experience considerable relief. A patient starting on hexamethonium must understand the importance of the details of the treatment, the fact that he will probably not feel as well as he would with his blood pressure higher, and that this is the price he must pay for the relative protection that the treatment gives. Patients with easy tendency to emesis should not be given protoveratrine.

Beyond these general considerations one may classify specific complications in terms of therapy as follows:

Conditions in which Treatment is Urgent and Often Successful

(a) *Left ventricular failure.* While acute pulmonary edema usually responds nicely to standard treatment, there are a residue of patients with severe hypertension in whom the reduction of peripheral resistance may turn the tide between life and death. If conventional measures have not brought relief within 20 minutes or half an hour in an individual with a blood pressure over 170 systolic, we believe that an attempt to lower the pressure to 120 by some such method is justified. The experience of Sarnoff *et al* with Arfonad infusions is cited as an example.[10] The drug is probably ideal in this situation because of its acute effect which can be easily regulated, over the short term. Hexamethonium or protoveratrine may also be used parenterally. If recovery occurs, intensive therapy must proceed with hexamethonium at first parenterally, then orally, or protoveratrine if severe uremia coexists. When the patient is out of failure and reasonably stabilized, decision as to sympathectomy can be made. If not azotemic these patients often do well following surgery although there is a somewhat increased operative risk.

(b) *Severe encephalopathy.* This may be due to cerebral hemorrhage or thrombosis, uremia or to acute "cerebral vasospasm." If there is a uremic odor to the breath or reason to suspect primary renal disease, and the pressure is very high, an attempted reduction with protoveratrine or Arfonad intravenously would be first choice. If stiff neck, headache, abrupt onset and blood in the spinal fluid point to cerebral hemorrhage and the pressure is still very high, one may resort to the very cautious administration of hexamethonium intravenously but it is uncertain whether one can stop the bleeding or do anything more than hasten exodus by this technic.

It is probably worth a trial, however, on the old presumption that if one lowers the blood pressure in severe cerebral hemorrhage, there is a greater chance of stopping the bleeding. If the attack is due to cerebral thrombosis either as evidenced by the gradual onset of neurologic signs, particularly in an older person with not too marked elevations of blood pressure, inhalation of carbon dioxide, injection of aminophylline intravenously, re-breathing into a paper bag may be tried but will probably not be very helpful. Lowering the blood pressure is contraindicated. If the pressure is very high, if the history suggests focal relatively reversible episodes in the past and renal failure is not apparent, gradual reduction of the systolic blood pressure to levels of 160 to 170 with intravenous hexamethonium may accomplish dramatic results. The same general principle applies to the treatment of encephalopathy accompanying acute nephritis or toxemia of pregnancy. In these two conditions protoveratrine or Arfonad are probably the drugs of choice for acute and maintenance treatment. When the focal encephalopathy is associated with the "benign" form of hypertension subsequent sympathectomy is clearly indicated after subsidence of the acute attack.

(c) *Retinopathy with impaired vision.* If the patient's renal function is not too seriously impaired, reduction of blood pressure with oral or parenteral hexamethonium to normotensive levels may over a period of two to three weeks result in sufficient resorption of exudates to permit restoration of near normal vision. Sympathectomy may then be considered and/or continued drug treatment. If renal function is impaired badly, intermittent treatment with oral protoveratrine as described above may be helpful.

(d) *Symptoms due to aneurysms in hypertensive patients.* Focal nerve palsies may result from dilatation of intracranial arteries. Hypertension may also cause aneurysms of the thorax. The renal function of these patients is not usually impaired and we have obtained gratifying results by lowering the systemic pressure by intensive parenteral hexamethonium therapy followed by outpatient oral treatment with this agent. Whether or not one can similarly "decompress" or postpone the rupture of an aneurysmal sac within the thorax is, of course, uncertain and will probably never be established but an attempt to lower the blood pressure in these conditions seems reasonable.

(e) *Malignant or premalignant hypertension.* In our experience this is the hypertensive emergency more likely to be neglected by the practitioner than any other. If a patient, particularly a young male, presents himself with diastolic blood pressures over 130 and particularly if hemorrhages or exudates appear in the eyegrounds, the probability of an ultimate malignant hypertension is great. We feel that this patient should have in rapid succession, sympathectomy, 200 mg. sodium diet, active inpatient treatment with hexamethonium with or without adjunctive drugs as necessary to lower the blood pressure to near normal levels and keep it that way. At the same time the renal function must be watched carefully. It is, at the moment, controversial whether reduction in pressure can protect against progressive nephrosclerosis, but the presumption is strong from: (1) the animal observations that the kidney protected by the clamp in Goldblatt hypertension does not undergo nephrosclerosis, (2) our experience with occasional patients with marginal renal function who have shown an arrest of their renal damage following lowering of the blood pressure with sympathectomy, (3) Schroeder's statistics with malignant hypertension and uremia where blood pressures have been strictly normalized for over two years. At this point it should be emphasized that by the time the NPN begins to rise substantially, damage has been done and treatment is not likely to be more than palliative. Consequently, it is the duty of the physician to recognize the setting in which malignant hypertension is likely to develop, and in such individuals survey renal function with some quantitative estimate, such as creatinine clearance, urea clearance, or PSP excretion at frequent intervals and start treatment without delay at the first sign of renal deterioration.

Conditions in which Hypotensive Therapy is Occasionally Successful

(a) *Early uremia.* With the NPN in the range of 60 to 80 mg. percent, hexamethonium with Apresoline, as mentioned above, may be helpful and certainly in the hands of Schroeder has appeared brilliantly successful. With more marked degrees of uremia these agents are difficult to administer, and protoveratrine may be of palliative value. It is doubtful whether hexamethonium should be given to hypertensive individuals with a blood pressure elevation secondary to chronic nephritis. Protoveratrine seems to be the drug of choice in this instance. Rauwolfia may be helpful. Sympathectomy is contraindicated.

(b) *Angina pectoris.* Sympathectomy is contraindicated unless one intends to do a cardiac denervation as well. To extend the procedure this far increases the mortality rate so much that it is likely to be prohibitive. Apresoline is contraindicated. Rauwolfia, in our experience, has had little effect on the condition. Protoveratrine

is sometimes successful. Hexamethonium may be attempted if the systolic pressure is usually over 180 or 190 in the hopes that the reduction in cardiac work will be greater than reduction in perfusion pressure in the coronary circuit. Great care must be exercised not to permit the blood pressure to fall too low under these circumstances. In general, angina pectoris is not accompanied by severe grades of hypertension and this problem seldom arises.

(c) *Sustained severe hypertension without major vascular complications.* We use as a definition of severe hypertension a systolic blood pressure almost continuously over 200 and a diastolic over 110. From our previous studies we know that the mortality rate in this condition will be 50 percent from hypertensive disease within 10 years. Whether or not drug therapy will be effective in reducing this mortality is uncertain. It has been established that sympathectomy improves the mortality rate under these circumstances. Therefore we recommend this as the treatment of first choice, urging it the more when there is evidence of the beginning of vascular disease such as cardiac enlargement, slight dyspnea, albuminuria or history of focal cerebral vascular episodes. If the patient has symptoms of headache, dizziness or tension, they are likely to be relieved by the surgery, and this is a further consideration. If the patient were over the age of 50 we would not advise surgery but would put him on a 200 mg. sodium diet with or without added rauwolfia. This might be the first step in a young individual although as stated before it is not certain whether he would keep up such a therapeutic program long enough to make a significant difference in his ultimate mortality rate. If surgery were refused or were unsuccessful, and symptoms persisted, we would be inclined to introduce Apresoline, hexamethonium, or rauwolfia, bearing in mind that the side effects of treatment must not be worse than the symptoms of the disease and must not interfere to a major degree with daily living since treatment must be made attractive enough to be persisted in for many years.

(d) *Early labile hypertension with blood pressures frequently near normal and occasionally above 200.* This is one of the most difficult conditions one is called upon to treat. Sympathectomy may be helpful although it seems drastic. We would prefer to wait until more sustained hypertension developed. Rauwolfia and dietary restriction would probably be the treatments of choice. In usual doses ganglionic blocking agents do not prevent pressor responses to environmental stimuli.

Conditions in which Hypotensive Therapy is useless or harmful:

The treatments described are useless or harmful in coronary thrombosis, hemiplegia, advanced uremia, cerebral thrombosis or arteriosclerosis even in the presence of severe grades of hypertension. It must be our objective as clinicians to foresee and prevent these advanced stages of degenerative vascular disease. It is the hope of the author that as more effective control of hypertension in its earlier stages is accomplished, these complications will occur with lessening frequency.

Conclusion

1. The principles and practice of treatment of hypertension are summarized.

2. The therapeutic indications are outlined for sympathectomy, low sodium diets, hydralazine, rauwolfia and veratrum alkaloids and ganglionic blocking agents.

3. The treatments of choice for hypertensive emergencies, certain kinds of hypertensive complications and for the so-called "benign" form of the disease are presented.

REFERENCES

1. Hoobler, S. W., Manning, J. T., Paine, W. G., McClellan, S. G., Helcher, P. O., Renfert, H., Jr., Peet, M. M., and Kahn, E. A.: The Effects of Splanchnicectomy on the Blood Pressure in Hypertension, *Circulation 4*:2, 173, 1951.
2. Grimson, K. S., Orgaine, E. S., Anderson B., D'Angelo, G. J.: Total Thoracic and Partial Lumbar Sympathectomy, Splanchnicectomy and Ciliac Ganglionectomy for Hypertension, *Ann. Surg. 138*:532, 1953.
3. Hoobler, S. W.: Personal Observations.
4. Schroeder, H. A.: *Hypertensive Diseases: Cause and Control,* Lea and Febiger, Philadelphia. 1953.
5. Hafkenschiel, J. H., Friedland, C. K., Yobaggy, J., and Crumpton, C. W.: Effects of 1-Hydrazinophthalazine on Cerebral Hemodynamics and Oxygen Metabolism in Hypertensive Subjects, *Pharmacol. Exp. Therap. 103*:345, 1951.
6. Hoobler, S. W., Corley, R. W., Kabza, T. G., and Loyke, H. F.: Treatment of Hypertension with Oral Protoveratrine, *Ann. Internal Med. 37*:465, 1952.
7. Morris, N.: Hexamethonium Compounds in the Treatment of Pre-eclampsia and Essential Hypertension During Pregnancy, *Lancet 1*:322, 1953.
8. Smirk, F. H.: Action of a New Methonium Compound in Arterial Hypertension, *Lancet 1*:457, 1953.
9. Smirk, F. H.: Practical Details of the Treatment of Hypertension by Hexamethonium Salts and by Pentamethylene 1:5 *bis* N (N-methyl pyrrolidinium) Bitartrate (M & B 2050A), *New Zealand Med. J. 52*:1, 1953.
10. Sarnoff, S. J., Goodale, W. T., and Sarnoff, L. C.: Graded Reduction of Arterial Pressure in Man by Means of a Thiophanium Derivative (RO 2-2222), *Circulation 6*:63, 1952.
11. Meilman, E. and Krayer, O.: Clinical Studies on Veratrum Alkaloids: II. The Dose-Response Relations of Protoveratrine in Hypertension, *Circulation 6*:212, 1952.

THE

PREPARATION OF

OPHTHALMIC MEDICATION

PART ONE

by JOHN A. SCIGLIANO AND MILTON W. SKOLAUT

THE THERAPEUTIC EFFECTIVENESS of ophthalmic medications may be altered, during the course of their preparation, by variables which are easily overlooked.

Problems to be considered and often associated with the compounding of this class of pharmaceuticals may be any or all of the following:

1. Sterilization Method
2. Contaminated Chemicals
3. Contaminated Glassware (including bottles)
4. Preparation Method
5. Distilled Water Source
6. Utilization of Buffer Systems
7. Use of Expiration Dating
8. Hydrogen Ion Concentration
9. Tonicity of Finished Product

Specifically in this study we sought to prepare ophthalmic solutions which would be relatively free of bacterial growth. Some data pertinent to other points enumerated above were observed during the course of this work and are briefly discussed later in the paper. These and the remainder of the problems should be subjects for future study.

Properties desired in sterilized ophthalmic solutions are that the preparations be made relatively free of micro-organisms in a short period of time and this condition maintained during and up to the expiration date: if the process be chemical sterilization, the agent should not be irritating and it should not be physiologically or chemically incompatible.

A study involving chemical sterilization of ophthalmic solutions has been reported in the literature.[1,2] The sterilizing agent used in the study was a quaternary ammonium compound, benzalkonium chloride,* in a single concentration of 1:5,000.

It has been stated that distilled water solutions of benzalkonium chloride are irritating to the

JOHN A. SCIGLIANO is Assistant Chief and MILTON W. SKOLAUT is Chief, both of the Pharmacy Department, Clinical Center, National Institutes of Health, Bethesda 14, Md.

Presented at the Annual Meeting of the American Society of Hospital Pharmacists, Salt Lake City, Utah, August 17 and 18, 1953.

*Zephiran Chloride, Winthrop-Stearns' brand of benzalkonium chloride, was used in this study.

Table I. Bacterial Counts of the Suspensions and of the Inocula

Organism	Count per ml.	Inoculum (0.15 ml.)
S. aureus	1,800,000	270,000
P. pyocyanea	29,550,000	4,432,500
E. coli	53,700,000	8,055,000

conjunctiva in concentrations greater than 1:-3,000.[3] Considering that more dilute solutions of benzalkonium chloride become less irritable as the concentration decreases, it was our desire to use this quaternary ammonium salt in various dilutions so as to determine by bacteriological methods the greatest dilution at which the optimum properties would be present in an ophthalmic solution. Essentially we desired to find the concentration which was capable of killing pathogenic bacteria in sufficiently high dilution as to be non-irritating and, more important, that the effect be produced rapidly.

Factors motivating such a study by hospital pharmacists are many. Of particular interest to us was the desire of knowing whether or not the organisms used in the cited work[1] had developed any resistance to benzalkonium chloride. Of more immediate concern was our desire, here in the Pharmacy Department, Clinical Center, to reduce to a minimum the number of variables affecting the ophthalmic solutions dispensed and/or administered to Clinical Center patients. Therefore, the following experimental work was performed and the resulting data are presented herewith.

Experimental

The organisms* used in this investigation were isolated from clinical material. They were *Staphylococcus aureus* (F.D.A. # 209), *Pseudomonas pyocyanea* (Lawson) and *Escherichia coli* (010 K5 L).

The controls were distilled water and an aqueous solution containing the alkaloids and chemicals. The dilutions of the sterilizing agent were 1:50,000, 1:30,000, 1:10,000 and 1:5,000 in distilled water. These were used as vehicles for the medications and/or buffers of test solutions 3, 4, 5, and 6, respectively.

The procedure[5] of this work was as follows: twenty-four (24) hour broth cultures of the organisms were made by inoculating Trypticase Soy Broth and incubating at 37°C. Bacterial counts of the suspensions were determined prior to the addition of inoculum to the solutions. The organism count was found by serial dilution and plating-out on Nutrient Agar. The bacterial counts of the suspensions appear above:

To three (3) ml. of each solution there was added the inoculum shown in Table I. Subcultures were made into Trypticase Soy Broth at intervals of 5 minutes, 30 minutes, 60 minutes, 2 weeks (except for all phases where *S. aureus* was the testing organism) and 4 weeks. Results were read after 24 hours incubation at 37°C.

All tubes demonstrating no growth were incubated an additional 24 hours for confirmation.

This study consisted of four phases of eight ophthalmic solutions each. All three organisms were inoculated into each of these 32 solutions. The phases divided the work according to the method used in the preparation of the solutions. Phase I may be referred to as the "Clean Technic." By this method the glassware was washed with a non-ionic detergent, rinsed with distilled water and ingredients weighed and the solution compounded with great care. Phase II may be referred to as the "Sterile Technic." In this method the plan of Phase I was followed except that all solutions and controls were sterilized by steam at 15 pounds pressure for 20 minutes. Phase III and IV followed plans similar to I and II, respectively, except that buffers were used and tonicity, in some instances, adjusted.

The solutions were prepared in distilled water and in distilled water plus buffer. These were as follows:

Medicament	Percent
Eucatropine Hydrochloride	1.0
Cocaine Hydrochloride	0.5
Pilocarpine Hydrochloride	2.0
Atropine Sulfate	2.0
Tetracaine Hydrochloride	0.5
Scopolamine Hydrobromide	0.25
Eserine Sulfate	0.25
Homatropine Hydrobromide	2.0

Formulas for these appear later in the paper.

Observations of the hydrogen ion concentration of each solution were made. The results appear in Table II below:

*These may be obtained by contacting Laboratory of Infectious Diseases, National Microbiological Institute, National Institutes of Health, Bethesda 14, Maryland.

TABLE II. HYDROGEN ION CONCENTRATION OF EACH SOLUTION

OPHTHALMIC SOLUTION	PHASE I & III	PHASE II & IV
	pH OR *pH* RANGE OF SOLUTIONS *(Readings are from left to right) (Solutions 2 thru 6 inclusive)*	
Eucatropine Hydrochloride 1%	4.88 to 5.28	6.7
Cocaine Hydrochloride 0.5%	4.83 to 5.22	4.76 to 5.24
Pilocarpine Hydrochloride 2%	4.18 to 4.84	6.32
Atropine Sulfate 2%	5.88 to 5.98	6.68
Tetracaine Hydrochloride 0.5%	4.98 to 5.78	6.68
Scopolamine Hydrobromide 0.25%	5.68 to 5.98	6.98
Eserine Sulfate 0.25%	6.12 to 6.22	3.75 to 4.7
Homatropine Hydrobromide 2%	5.02 to 5.40	6.52 to 6.34

Results

The data obtained from this study was tabulated for each solution. This will be found in Table III.

Discussion

Upon examination of the tabulated data, it was noted that in most instances the 1:10,000 concentration of benzalkonium chloride had an effective killing power after the organisms had been in contact with it for 30 minutes. Exceptions to this were observed with atropine sulfate in the buffered phases. The unbuffered phases of atropine sulfate showed the organisms to be killed after 30 minutes contact with the 1:10,000 concentration of the agent.

The buffered phases of eserine sulfate solutions all supported growth, whereas the distilled water solutions of this alkaloid showed effective killing of the organisms, in some instances, even where the organisms had been in contact with the 1:-50,000 dilution for 30 minutes. Growth was absent here in the 1:50,000 in many instances after 5 minute contacts between agent and organisms.

Cocaine hydrochloride solutions which were buffered with boric acid showed none of the effects expected from the chemical incompatibility between boric acid and benzalkonium chloride.

Observations showed all controls to have supported growth.

Nearly all tetracaine hydrochloride solutions exhibited no growth in the subcultures. Even the control which did not contain benzalkonium chloride had inhibited growth in the subculture tubes. Investigating this apparent peculiarity, wherein tetracaine hydrochloride seemed to exhibit bactericidal properties, it was concluded that the tablets of tetracaine hydrochloride used in the preparation of these ophthalmic solutions may contain a bactericide in their formulation.

Unbuffered solutions of eserine sulfate exhibited more nearly the desired properties than did the buffered solutions. The solutions of eserine sulfate which were steam sterilized assumed a deep red color and became somewhat turbid, this latter most noticeable in solutions containing benzalkonium chloride in concentrations of 1:10,000 and 1:5,000. Eserine sulfate solutions which were not steam sterilized showed only a slight pink coloration. Here, also, the solutions containing benzalkonium chloride in concentrations of 1:10,000 and 1:5,000 were somewhat cloudy.

Formulas[2]

Following are formulas recommended for use based on findings of this study:

1. Eucatropine Hydrochloride 1.0 Gm.
   Benzalkonium Chloride
   Solution 1:10,000, to make 100.0 cc.

2. Eucatropine Hydrochloride 1.0 Gm.
   NaH_2PO_4, anhydrous 0.4 Gm.
   Na_2HPO_4, anhydrous 0.47 Gm.
   Benzalkonium Chloride Solution 1:10,000 to make 100.0 cc.

3. Cocaine Hydrochloride 0.5 Gm.
   Benzalkonium Chloride
   Solution 1:10,000, to make 100.0 cc.

4. Pilocarpine Hydrochloride 2.0 Gm.
   Benzalkonium Chloride
   Solution 1:10,000, to make 100.0 cc.

5. Pilocarpine Hydrochloride 2.0 Gm.
   NaH_2PO_4, anhydrous 0.4 Gm.
   Na_2HPO_4, anhydrous 0.47 Gm.
   NaCl 0.26 Gm.
   Benzalkonium Chloride
   Solution 1:10,000, to make 100.0 cc.

Table III. Effect of Various Concentrations of Benzalkonium Chloride upon Micro-Organisms in Selected Ophthalmic Solutions

EUCATROPINE HYDROCHLORIDE 1% SOLUTION

	PHASE I												PHASE II											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	+	–		+	+	+	–		+	+	–	–		+	+	+	–		+	+	+	–		+	+	–	–	
4	+	+	+	–		+	–	–	–		+	–	–	–		+	+	+	–		+	+	+	–		+	+	–	–	
5	+	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

	PHASE III												PHASE IV											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	+	–		–	–	–	–		+	+	+	+		+	+	+	–		–	–	–	–		+	+	+	+	
4	–	–	–	–		–	–	–	–		+	+	–	–		–	–	–	–		–	–	–	–		+	+	–	–	
5	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

COCAINE HYDROCHLORIDE 0.5% SOLUTION

	PHASE I												PHASE II											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	+	–		–	–	–	–		+	–	–	–		+	+	+	–		+	+	+	–		–	–	–	–	
4	+	+	–	–		–	–	–	–		–	–	–	–		+	+	–	–		+	–	–	–		–	–	–	–	
5	+	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

	PHASE III												PHASE IV											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	+	–		–	–	–	–		+	+	+	–		+	+	+	–		–	–	–	–		–	–	–	–	
4	+	+	–	–		–	–	–	–		–	–	–	–		+	+	–	–		–	–	–	–		–	–	–	–	
5	+	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

PILOCARPINE H Cl 2% SOLUTION

	PHASE I												PHASE II											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	–	–	–		+	–	–	–		–	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
4	+	–	–	–		+	–	–	–		–	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
5	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

	PHASE III												PHASE IV											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	–	–	–		+	–	–	–		–	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
4	+	–	–	–		+	–	–	–		–	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
5	+	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

ATROPINE SULFATE 2% SOLUTION

	PHASE I												PHASE II											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	–	–		+	–	–	–		–	–	–	–		+	+	+	–		+	–	–	–		–	–	–	–	
4	+	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
5	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

	PHASE III												PHASE IV											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	+	–		+	–	–	–		–	–	–	–		+	+	+	–		+	–	–	–		–	–	–	–	
4	+	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
5	+	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

TETRACAINE HYDROCHLORIDE 0.5% SOLUTION

	PHASE I												PHASE II											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	–	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
3	–	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
4	–	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
5	–	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	

	PHASE III												PHASE IV											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	–	–	–		+	–	–	–		+	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
3	–	–	–	–		+	–	–	–		+	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
4	–	–	–	–		+	–	–	–		+	–	–	–		+	–	–	–		+	–	–	–		–	–	–	–	
5	–	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

SCOPOLAMINE HYDROBROMIDE 0.25% SOLUTION

	PHASE I												PHASE II											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	+	–		+	+	–	–		+	+	–	–		+	+	+	–		+	+	–	–		+	+	–	–	
4	+	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
5	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

	PHASE III												PHASE IV											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	+	–		+	+	–	–		+	+	–	–		+	+	+	–		+	+	–	–		+	+	–	–	
4	+	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
5	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

ESERINE SULFATE 0.25% SOLUTION

	PHASE I												PHASE II											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		–	–	–	–		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	–	–	–		–	–	–	–		+	–	–	–		+	+	+	+		+	+	+	+		+	+	+	+	
4	–	–	–	–		–	–	–	–		–	–	–	–		+	+	+	+		+	+	+	+		+	+	+	+	
5	–	–	–	–		–	–	–	–		–	–	–	–		+	+	+	+		+	+	+	+		+	+	+	+	
6	–	–	–	–		–	–	–	–		–	–	–	–		+	+	+	+		+	+	+	+		+	+	+	+	

	PHASE III												PHASE IV											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
4	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
5	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
6	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	

HOMATROPINE HYDROBROMIDE 2% SOLUTION

	PHASE I												PHASE II											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	–	–		+	–	–	–		–	–	–	–		+	+	+	–		+	–	–	–		–	–	–	–	
4	–	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
5	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

	PHASE III												PHASE IV											
	S. AUREUS					E. COLI					P. PYOCYANEA					S. AUREUS					E. COLI					P. PYOCYANEA				
	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W	5	30	60	2W	4W
1	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
2	+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+		+	+	+	+	
3	+	+	–	–		+	–	–	–		–	–	–	–		+	+	+	–		+	–	–	–		–	–	–	–	
4	–	–	–	–		–	–	–	–		–	–	–	–		+	–	–	–		–	–	–	–		–	–	–	–	
5	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	
6	–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–		–	–	–	–	

CODE: 1 = DISTILLED WATER (CONTROL)
2 = DISTILLED WATER SOLUTION OF DRUG (CONTROL)
3 = BENZALKONIUM CHLORIDE 1:50,000
4 = BENZALKONIUM CHLORIDE 1:30,000
5 = BENZALKONIUM CHLORIDE 1:10,000
6 = BENZALKONIUM CHLORIDE 1:5,000

(+) = GROWTH (–) = NO GROWTH
5 = CONTACT WITH AGENT 5 MINUTES
30 = CONTACT WITH AGENT 30 MINUTES
60 = CONTACT WITH AGENT 60 MINUTES
2W = CONTACT WITH AGENT 2 WEEKS
4W = CONTACT WITH AGENT 4 WEEKS

6. Atropine Sulfate	2.0	Gm.
Benzalkonium Chloride Solution 1:10,000, to make	100.0	cc.
7. Tetracaine Hydrochloride*	0.5	Gm.
KH_2PO_4, anhydrous	0.43	Gm.
Na_2HPO_4, anhydrous	0.57	Gm.
NaCl	0.34	Gm.
Distilled Water, to make	100.0	cc.
8. Tetracaine Hydrochloride	0.5	Gm.
Distilled Water, to make	100.0	cc.
9. Scopolamine Hydrobromide	0.25	Gm.
KH_2PO_4, anhydrous	0.19	Gm.
Na_2HPO_4, anhydrous	0.81	Gm.
NaCl	0.33	Gm.
Benzalkonium Chloride Solution 1:10,000, to make	100.0	cc.
10. Scopolamine Hydrobromide	0.25	Gm.
Benzalkonium Chloride Solution 1:10,000, to make	100.0	cc.
11. Eserine Sulfate	0.25	Gm.
Sodium Bisulphite	0.1	Gm.
Benzalkonium Chloride Solution 1:10,000, to make	100.0	cc.
12. Homatropine Hydrobromide	2.0	Gm.
Benzalkonium Chloride Solution 1:10,000, to make	100.0	cc.
13. Homatropine Hydrobromide	2.0	Gm.
NaH_2PO_4, anhydrous	0.4	Gm.
Na_2HPO_4, anhydrous	0.47	Gm.
NaCl	0.1	Gm.
Benzalkonium Chloride Solution 1:10,000, to make	100.0	cc.

Various chemicals contain spores of micro-organisms in their original state as purchased. The spores cause no trouble in many classes of pharmaceuticals and not too generally even in ophthalmic solutions. However, ophthalmic solutions used prior to or following eye surgery or in cases of infections should be free of micro-organisms.

No less important are spores or micro-organisms, fungi, etc., which may be present in empty or new bottles. These may be introduced during shipment or during storage or handling. Ophthalmic solutions as appear in the preceding formulas will eliminate such organisms.

Freshly distilled water should be used in the compounding of all these pharmaceutical preparations.

*Pontocaine Hydrochloride Tablets, Winthrop-Stearns' brand of Tetracaine for making ophthalmic solutions.

The phosphate buffers published in an earlier paper[6] were again used. No other investigations were made into any buffer systems in this study.

Ophthalmic solutions are generally buffered for two reasons. They may be buffered to a *p*H yielding a preparation which is comfortable to the patient, but this usually decreases the stability of the solution. They also may be buffered to stabilize the active alkaloid at a *p*H as low as 2.5 which is irritating to the eye. Another factor to consider is the reduction in activity of the benzalkonium chloride by the introduction of micro-organisms with repeated use. Taking these factors into consideration, ophthalmic solutions should carry an expiration date label. This dating should conform with a predetermined "shelf life," which can be accomplished in actual practice by attaching a supplemental label bearing the following: "Do Not Use After_____," and by dispensing in such quantities as to insure usage within the "shelf life."

Conclusions

The results of this work showed benzalkonium chloride capable of freeing ophthalmic solutions of micro-organisms in a short period of time and maintaining this condition from time of compounding to the expiration date. The use of benzalkonium chloride 1:10,000 in solutions intended to be instilled in the eye appeared to be adequate.

There remain numerous other problems involved in the preparation of ophthalmic medications for future investigation.

LITERATURE CITED

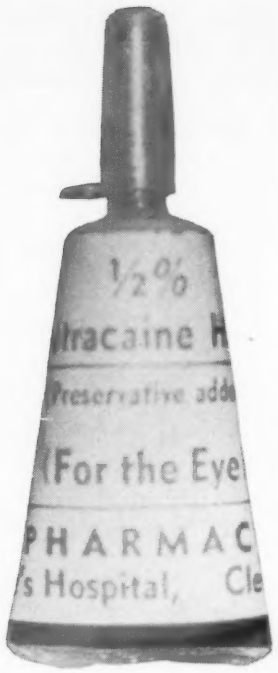
1. McPherson, S. D. and Wood, R. M.: Self-Sterilizing Ophthalmic Solution, *Am. J. Ophthalmol. 32*:675 (May) 1949.
2. Skolaut, M. W., Ophthalmic Medications, *Bull. Am. Soc. Hosp. Pharm. 5*:172 (July-Aug.) 1948.
3. *Zephiran Chloride*, (Brochure), Winthrop-Stearns, Inc., New York, N. Y.
4. *Products for the Bacteriological Laboratory*, (Booklet) Baltimore Biological Laboratory, Baltimore, Md.
5. Scigliano, J. A., *et al*: Fungicidal Testing of Some Organo-Copper Compounds, *J. Am. Pharm. Assoc., Sci. Ed. 39*:673 (Dec.) 1950.
6. Hind, H. W. and Goyan, F.M.: A New Concept of the Role of Hydrogen Ion Concentration and Buffer Systems in the Preparation of Ophthalmic Solutions, *J. Am. Pharm. Assoc., Sci. Ed. 36*:33 (Feb.) 1947.

ACKNOWLEDGMENTS

The authors wish to acknowledge the generous assistance of Dr. Karl Habel, Chief, Laboratory of Infectious Diseases, National Microbiological Institute, National Institutes of Health, for laboratory facilities; Dr. Elizabeth Verder, Senior Bacteriologist, for consultations and organisms; and Mr. Horace C. Turner for assistance in the laboratory.

by WAI-YING WU *and* BETTY K. JOB

polyethylene tubes for solutions



SINCE THERE IS ALWAYS THE POSSIBILITY of contaminating eye solutions by replacing the eye dropper back into the bottle after using, we in this hospital have tried and found it satisfactory to dispense ophthalmic solutions in small individual polyethylene dropper tubes instead of dropper bottles.

These polyethylene tubes are flexible and have a small capped dropper mouth. They similate the ophthalmic ointment collapsible tubes in shape and each holds about 4 cc. of solution. Eye solutions can be applied simply by squeezing the tube while holding it above the eye in an inverted position. The tapered tip, being more rigid than the body of the tube, delivers the solution right into the eye drop by drop like glass droppers. After using, the tight fitted cap may be put back on the tip thus preventing contamination of the solution and eliminating the problem of keeping the droppers clean. Due to the fact that the tubes are made of polyethylene and are nonbreakable, the possible danger of chipped glass dropper tips contacting the eye is avoided. Also, expensive medication is not lost in the separate dropper since the solution is dropped directly from the container.

To clean and chemically sterilize tubes which are used for eye solutions using benzalkonium chloride as a preservative, we fill them with benzalkonium chloride 1:5,000 solution and then allow them to remain in this solution until they are needed for use. Tubes for ophthalmic solutions in which other preservatives are used should, of course, be allowed to stand in a like preservative solution.

Self-sterilizing eye solutions can be dispensed in tubes rinsed with distilled water. Polyethylene tubes will melt on autoclaving.

The tubes are tested for leaks by capping and applying pressure to the sides. When the tubes have been tested they are emptied and then filled immediately with the solution to be dispensed. When ready to be filled, the tube is held between the thumb and the forefinger and pressure is applied by squeezing. Then the tip of the tube is dipped into the medicated solution and the pressure is released. The vacuum creates a suction thus drawing the solution into the tube. One squeeze will suck in from 3 to 4 cc. of the solution, depending on the force applied. Material might be saved by filling the tubes with a needle. More solution may be put in the tubes by this method, but we find it time-consuming and impractical, due to difficulties caused by the size of the hole in the mouth of the dropper.

(*Continued on page 72*)

WAI-YING WU is Intern Pharmacist and BETTY K. JOB is Assistant Chief Pharmacist, both at St. Luke's Hospital, Cleveland, Ohio.

The Pharmacist in Today's Hospital

by CHARLES U. LETOURNEAU

THE SOCIAL AND ECONOMIC DEVELOPMENT of our times has brought about some important changes in the manners and customs of our people. In line with these changes, the practice of medicine, which was confined largely to home and office visits, has become a team undertaking with such a complexity of pattern that it is difficult in many instances to isolate the doctor-patient relationship to determine the extent of responsibility of the physician to the patient. Concepts of nursing have similarly metamorphosed with the professional nurse rapidly assuming the quality of nursing team supervisor instead of personal servant to the patient. The development of the hospital is largely responsible for these changes and it, in turn, can trace its growth to the dramatic scientific discoveries of the past century.

Trends Affecting Pharmacy

Pharmacy has been affected likewise by these changes. The practice of pharmacy has progressed a long way since it was defined as "the art of preparing, preserving and compounding medicine according to the prescriptions of the physicians." To be sure, this definition still forms the basis for the practice of pharmacy but today's pharmacist needs to know so much more than the fundamentals of his profession that this narrow definition restricts the scope of the pharmacist and prevents a fair evaluation of his contribution to the health of the people.

CHARLES U. LETOURNEAU, M.D., is Secretary of The Council on Professional Practice, American Hospital Association, Chicago.

More and more pharmacists are now practicing in hospitals, a trend that is in keeping with the times. This trend has been noted in medicine, nursing, social service and other paramedical professions, some of which practice exclusively in hospitals.

In the early days of hospital development, pharmacies were included in hospitals for the sake of convenience. Hospitals with a large volume of prescriptions, many of them free, employed a pharmacist to compound, preserve and dispense medicines in much the same manner as the commercial pharmacist did for prescriptions outside the hospital. In many respects the pharmacist was left to his own devices, usually in the cellar, in some converted storage space; a situation which was accepted with stoic philosophy as a necessary evil of the circumstances. He was respected as a man who knew his job and with true professional zeal he kept the secrets of his profession religiously to himself. Nor did anyone seek to pry into them as the pharmacy was taboo and few were

permitted to venture within its sacrosanct portals. By the same token, the pharmacist rarely ventured out of his pharmacy. Having provided the drugs and the medicines that were asked for, he considered his responsibilities ended with the correct compounding and labeling of the containers. He was rarely asked for and rarely gave advice. Professional pride prevented physicians from asking his opinion for fear of displaying their ignorance and the same was true of the nursing profession. Fear of being accused of practicing medicine also tended to make the pharmacist taciturn with outpatients who came to his pharmacy to get prescriptions filled. Relationships with physicians in these instances were delicate as physicians were highly sensitive to queries about their prescriptions. The pharmacist, like other professional groups in the hospital, was compartmented and guarded his prerogatives jealously, being careful at the same time not to encroach on the prerogatives of others.

The Modern Hospital Pharmacist

The conditions that brought about these attitudes no longer exist. Most physicians realize today that the length and breadth of medical knowledge is so vast that it is impossible for any physician to know it all. The public demand for professional nursing services has likewise become so great as to be impossible to meet. The nursing profession realizes that the nurse must shed many of the responsibilities once considered within the exclusive jurisdiction of nursing. The partnership of these professions with the pharmacist, once shunned, is now more than welcome, it is sought for eagerly. The pharmacist in today's hospital is a partner on the professional staff who takes rank and precedence equal to medicine, nursing, physical therapy, administration and dietetics, to mention but a few. He has finally assumed his rightful position as a member of the hospital team by asserting his claim to recognition. He has knowledge that no one else can provide and has an important contribution to make to the welfare of the patient.

Primarily, the pharmacist in today's hospital is still responsible for preparing, preserving and compounding medicines according to the prescriptions of physicians. With the development of the large pharmaceutical corporations, however, the physical labor of preparing, preserving and compounding medicines has been largely taken out of the hands of the individual pharmacist. In some ways this is a good thing; in other ways it is less desirable. From the administrative point of view, it relieves hospitals of liability for mistakes in the manufacturing of medicines since, by law, the manufacturer warrants his product. Although largely relieved of the physical labor of manufacturing, the pharmacist has acquired an even greater responsibility in this area, that of identifying the chemical substances under their various trade names and of distinguishing between the variations in composition of substances designed to produce the same or similar therapeutic effects. Thus, the pharmacist of today requires a much greater knowledge of pharmacology than did his forefathers.

In the larger hospitals, physicians who are specialists in pharmacology may be available and thus relieve the pharmacist of this responsibility, but the average physician is unable to keep up with the developments in the pharmaceutical field and must rely on his partner, the pharmacist, to help him in the selection of the proper drug. This assistance has been supplied all too often by the pharmaceutical representative, who, naturally, places his own product in the best possible light and cannot give the same objective evaluation that can be given by the pharmacist. In the field of barbiturates alone, to select a common example, new products appear on the market almost daily, supported by exaggerated claims which serve to confuse rather than assist the physician. The physician in today's hospital seeks the advice of the pharmacist on every new product and the pharmacist must be prepared to explain in what way the new product differs from other products already in the field. If he cannot do this, the pharmacist is not living up to his modern responsibilities.

Pharmacy Committee Responsibilities

Every well organized hospital has a Pharmacy Committee of the medical staff. Ex-officio, the hospital pharmacist is a member and secretary of this committee, or should be. The main function of the Pharmacy Committee is to evaluate new products and maintain the hospital formulary up to date. In this committee the pharmacist has much to say. He should be prepared to give comparative analyses on all new products under consideration bearing in mind their therapeutic benefits, and the qualifications of physicians on the staff of the hospital to use the new drugs safely. This latter is often a delicate matter since it may impugn the professional capacities of a member of the medical staff. Yet, within the confines of the Pharmacy Committee it can be and should be discussed frankly and honestly. Such hazardous drugs as dicumarol, ACTH and streptomycin are not for use by the untrained. The Pharmacy Committee should establish the fact that all physicians on the hospital staff are entirely fa-

miliar with the dangerous aspects of new drugs or restrict their use to certain physicians.

In the field of narcotics, the hospital pharmacist now has a legal responsibility which far transcends that of the commercial druggist. Ordering as he does in large quantities, he may be criminally liable for failure to account for the disposal of narcotics satisfactorily. Although he is acting on behalf of the hospital, he is often the only person in the hospital administration with the professional qualifications to assume responsibility for the narcotics. This being the case, it is no longer sufficient as of old for the pharmacist to prepare and dispense narcotic drugs and then wash his hands of responsibility for their final disposal. He must now extend his jurisdiction beyond the doors of the pharmacy and assure himself that narcotics have been disposed of only on the order of a physician. Discrepancies and deviations must be reported at once to the administration of the hospital and accounted for without undue delay. An investigation should be initiated by the Pharmacy Committee and a report submitted to the administrator for whatever action is deemed necessary under the circumstances.

Safety Promotion

The pharmacist in today's hospital is a safety expert. Such mundane matters as the proper labeling and identification of drugs, solutions and antiseptics are matters of the utmost importance. Errors in identification of medicines have proven to be fertile sources of litigation in the past. Although there are laws and regulations galore designed to prevent mistakes, these still occur with painful frequency. The pharmacist should call to the attention of the administration and the medical staff the hazards inherent in the improper storage of alcohols and inflammables and insist that the laws concerning these substances be complied with. The elimination of hazards pertaining to his particular profession is one of the duties of the modern hospital pharmacist. Such chemical substances as boric acid, still in use in some hospitals, should be done away with as they have been eliminated from stock in many of our more progressive hospitals.

Because he possesses highly specialized knowledge about drug laws and pharmaceutical standards he must take the initiative in informing the administration and the medical staff of any changes in these. He must insist upon compliance with the laws and nationally recognized standards. His stock should conform to the U.S.P., N.F. and N.N.R. listings and he should call attention to any deviations from these.

Management Functions

In the area of administration, the hospital pharmacist must be a combined accountant, purchasing agent, production engineer, store man and distributor. Where a separate purchasing service is provided, the hospital pharmacist is responsible for preparing the specifications of items to be purchased. More than likely he will have to indicate the sources of supply. He must prepare the annual budget for the pharmacy and fix charges to the patients for drugs according to the policy agreed upon with the hospital administrator. He must schedule production according to the hospital's needs and ensure that there is sufficient stock on hand. Finally he must arrange to distribute requirements regularly and efficiently. Among his intangible responsibilities are his relationships with the other departments, with the professions, with the administration and with the patients. At all times he must be a smooth diplomat even under the most adverse circumstances, and should be endowed with the patience of Job.

Educational Duties

Today's hospital pharmacist has extensive educational duties. In the larger hospitals, he is charged with teaching interns how to write prescriptions. He instructs the student nurses in materia medica and where schools for paramedical professions exist, he lectures to medical record librarians, physical therapists, dietitians, medical social workers, and laboratory and x-ray technicians according to their needs.

At definite intervals during the year, the hospital pharmacist reviews new pharmaceutical products at clinical staff meetings and whenever necessary for the nursing and associated professional staffs. He is also expected to participate in the hospital program for public education and should be prepared from time to time to address the local service clubs or meetings of the women's hospital auxiliary. Public relations is a hospital duty that must be shared by everyone.

The pharmacist in today's hospital is one of the most important partners in the health team. In the large hospital, his functions may be purely advisory and administrative; in the small hospital he may be the general factotum who doubles in brass as administrator, purchasing agent, accountant and errand boy. But whatever the size of the hospital in which he operates, the pharmacist is today achieving long overdue recognition of his importance to the patients, to the physicians, to the hospital, and to the people. And in return he can derive an enormous satisfaction for a contribution well made to the service of humanity.

Hospital Pharmacy in COSTA RICA

as reported to

ANNA MAY ORELLANA, *former pharmacist at Midway Hospital St. Paul, Minnesota, U. S. A.*

by

LIC. C. CASTRO P., Director of the Department of Pharmacy of the Ministry of Public Health of Costa Rica

LIC. R. MONTERO G., Chief Pharmacist of the Seguro Social Pharmacies of Costa Rica

LIC. AGRIPINA DE BARRIONUEVO, Chief Pharmacist in the Laboratory for the Manufacture of Injectables, San Juan de Dios Hospital

LIC. MARIA JULIA UMANA, Pharmacist in the Laboratory for the Manufacture of Injectables, San Juan de Dios Hospital

LIC. ELSA MARIA PEREZ, Chief Pharmacist, San Juan de Dios Hospital

LIC. MARIA ADELA OCAMPO, Pharmacist, San Juan de Dios Hospital

LIC. DEODONO GONZALEZ, Pharmacist, United Fruit Company Hospital, Golfito

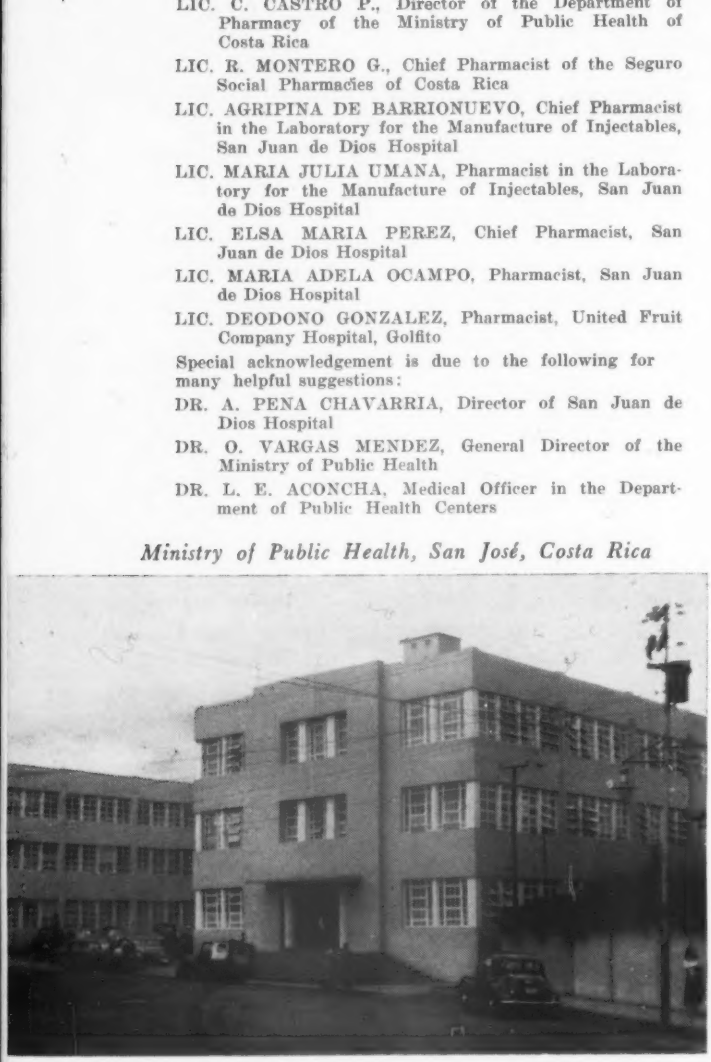
Special acknowledgement is due to the following for many helpful suggestions:

DR. A. PENA CHAVARRIA, Director of San Juan de Dios Hospital

DR. O. VARGAS MENDEZ, General Director of the Ministry of Public Health

DR. L. E. ACONCHA, Medical Officer in the Department of Public Health Centers

Ministry of Public Health, San José, Costa Rica



THE CENTRAL AMERICAN REPUBLIC of Costa Rica is bounded by Nicaragua to the north, the Caribbean Sea to the east, Panama to the south, and the Pacific Ocean to the west. Of a total population of 881,313 inhabitants, 306,415 reside in the province of San José, which contains the capital city. This distribution makes it possible to have a centralization of hospital pharmaceutical services, as will be pointed out later.

Educational Requirements of a Pharmacist

The training of a pharmacist in Costa Rica consists of four years' study in the pharmacy school at the university plus two years of practical experience obtained under the direction of a licensed pharmacist. Then, after passing an examination, the student receives his license and becomes a member of the College of Pharmacists.

Pharmaceutical Legislation

The College of Pharmacists presents pharmaceutical laws through the Ministry of Public Health to the legislative assembly for its approval. Article 9 of the Regulations for Pharmaceutical Establishments of 1946 states that all pharmaceutical establishments must be staffed by a professional person who is a member of the College of Pharmacists of Costa Rica. Exceptions to this rule are the dispensaries of the doctors or dispensaries in isolated places where there are no drug stores staffed by licensed pharmacists. Article 99 of Law No. 809, November 2, 1949 of the Sanitary Code states that hospitals, sanatoriums, rest homes, clinics, preventoriums, maternity clinics, etc., as well as barracks and prisons, may establish pharmacies or dispensaries to cover their own needs and they may be staffed by a licensed pharmacist or not, according to the ruling by the College of Pharmacists. At present there are about 44 pharmacists employed in hospitals and dispensaries throughout the country.

Types of Medical Care

Medical care in Costa Rica may be classified as follows:

Outpatient Dispensary, United Fruit Company Hospital at Golfito

1. Charitable. (Sponsored by the government, one of the sources of income being the national lottery.)
   a. Medical care through hospitals and dispensaries.
   b. Public health centers.
2. Seguro Social. (Government insurance plan for the employed.)
3. Private.

All hospitals, clinics, dispensaries, etc. in the country must meet the requirements specified by the Ministry of Public Health.

National Hospital System of the Ministry of Public Health

The National Hospital System under the Ministry of Public Health is as follows:

1. Central Hospital (1,474 beds): San Juan de Dios Hospital in San José, 4 pharmacists.
2. Regional hospitals (833 beds): Alajuela, 2 pharmacists; Cartago, 1 pharmacist; Heredia, 1 pharmacist; Liberia, 1 pharmacist; and Puntarenas, 1 pharmacist.
3. Five outlying hospitals (219 beds): only the hospital at Puerto Cortés has a pharmacist.
4. Sixteen rural centers of medical care (Dispensaries) (192 beds).
5. Centers of special medical care (1,336 beds):
   a. Instituto Materno Infantil "Carit" (Maternity), San José.
   b. Asilo Chapui (mental institution), San José, serviced by pharmacy of San Juan de Dios Hospital.
   c. Sanatorio R. Chacon Paut (neuropsychiatry), Tres Ríos.
   d. Sanatorio Nacional "Las Mercedes" (leprosy), Curridabat, 1 pharmacist.
   e. Sanatorio "Carlos Duran" (tuberculosis), Tierra Blanca, 1 pharmacist.
   f. Preventorio Roosevelt (incipient tuberculosis), Coronado.

Charitable and private care both are available in all five classes. However, free care is only for the indigent in the first four classes, whereas anyone may receive free care in the fifth class.

The National Hospital Formulary

The first *National Hospital Formulary* was accepted in 1938 by the Ministry of Public Health when it was under the direction of Dr. Peña Chavarria.[1] It contains formulas taken from the formularies of all the hospitals in the country as well as from foreign formularies.

The hospitals and medical care centers of the National Hospital System dispense only drugs in the *National Hospital Formulary* of Costa Rica. The latest edition of this has been compiled by Lic. C. Castro Porras, Director of the Department of Pharmacy (created in 1936) of the Ministry of Public Health. Under his direction in the central pharmacy of the Ministry in San José these formulas are compounded and monthly supplies are sent to each hospital or center which does not have a pharmacist. Here, also, an average of 5,000 prescriptions a month is filled for people from the suburbs of San José and from nearby villages.

Public Health Centers

The public health centers also receive their pharmaceutical supplies monthly from the central pharmacy of the Ministry in San José. The formulary used in these centers is compiled by Lic. Castro. It is much smaller than the hospital formulary as the centers promote preventive medicine and are not for treatment. They have well-baby clinics for prenatal care, and others.

San Juan de Dios Hospital

San Juan de Dios Hospital in San José, the central hospital of the National Hospital System, was founded in 1852. It has 1,424 free beds for those referred to it by the medical care centers (dispensaries) throughout the country or by its own outpatient clinic for residents of San José. It also has a small section of 50 beds for private patients.

The first licensed pharmacist was employed at San Juan de Dios Hospital in 1943. Prior to this the pharmacy was in charge of a trained Sister of Charity supervised by pharmacists acting as advisors. Appointments are made by the administrator and, thus far, no special examination is required. The present staff consists of four registered pharmacists and 13 assistants. When the pharmacists are not on duty on Sundays, holidays, and evenings, a Sister of Charity is in the pharmacy. In case of emergency one of the pharmacists is called.

The pharmacy is divided into a dispensing section for inpatient and outpatient prescriptions (24,000 prescriptions per month), a manufacturing section, a storeroom, and a laboratory for the preparation of injectibles. The medical staff is restricted to the *National Hospital Formulary,* many of the items of which are manufactured in the pharmacy. There are very few stock supplies of drugs on the wards.

The laboratory for injectibles has been separated from the rest of the pharmacy and has its own staff. Eventually this laboratory will prepare parenteral solutions for all of the hospitals in the National Hospital System. Lic. Marie Julia Umaña of this department is the only hospital pharmacist who also teaches. She is an instructor in the Hospital's School of Nursing where she gives a course in "Introduction to Materia Medica."

Seguro Social System.

The Seguro Social System of government insurance for employed people began in 1942. All of Costa Rica is not yet covered by the system although gradually new zones are being added. At present mainly the central part of the country where the population is most concentrated is included. In 1952 there were 135,000 persons carrying maternity and illness insurance. Of these, 71,500 have insurance only for the worker while 63,000 have insurance for the worker and also for his family.

All workers in the zones covered by Seguro Social and earning 400 colones a month or less are required by law to be insured. For those earning over 400 colones a month insurance is optional and depends upon the agreement of the worker and employer.

The employer, the employee, and the government pay a percentage of the salary of the insured person to the Seguro Social each month. For a worker only, the employer and employee each pay 3 percent and the government pays 1 percent. For a worker and his family, the employer and employee each pay 4 percent and the government 2 percent.

While sick or hospitalized the employee receives half salary for a period not to exceed 26 weeks. All medical care and hospital bills are paid in full without limit up to one year for one illness.

Seguro Social has two hospitals and 19 dispensaries throughout the country, each hospital and dispensary being staffed by licensed pharmacists. All of these branch pharmacies are under the control of the central pharmacy in the hospital in San José. The total number of beds available in Seguro Social hospitals is 400, of which 350 are in the central hospital in San José and 50 in the hospital in Turrialba. In emergencies the insured patients may be admitted to other hospitals and the expenses are covered by the Seguro Social organization. Likewise, the Seguro Social hospital in Turrialba will accept noninsured cases in emergencies.

The central pharmacy of the Seguro Social has five licensed pharmacists and 40 assistants, all selected by competitive examination. According to Chief Pharmacist R. Montero G., it is divided into the following departments:

1. Central pharmacy (outpatient and inpatient service):

Here are filled all the prescriptions for the hospitalized cases as well as for those outpatients from San José and suburbs. In 1952 a total of 439,288 prescriptions was filled (36,607 monthly or 1,407 daily). There are no stock supplies of drugs throughout the hospital. Everything that leaves the pharmacy is only by written order of the doctor for a specific patient. This necessitates 24 hour duty by the pharmacists, but they

feel this is required in order to eliminate the chances of error in dispensing by nontrained personnel.

2. Pharmacy laboratory:
All of the manufacturing for the hospitals and dispensaries throughout the country is done in the laboratory of the Central Pharmacy. Many formulas are prepared which are similar to those of imported specialties. Also many original formulas have been developed in order to fill the needs of the medical staff. At present intravenous solutions are not manufactured, although it is planned to do so when space becomes available.

3. Pharmacy storeroom:
A perpetual inventory is kept of all the stock on hand.

4. Room for packaging and bottling the manufactured products.

5. Branch pharmacies of hospitals and dispensaries:
The administration of all of these pharmacies is under the direction of Lic. Montero of the central pharmacy. The branches are only for dispensing and do no manufacturing. In 1952 they filled 350,769 prescriptions.

6. General card file of branch pharmacies:
In the central pharmacy is kept a record of the stock on hand in each branch pharmacy throughout the country. Each branch orders supplies every month from the central pharmacy. Monthly inventories are taken in each pharmacy and are sent to the central pharmacy together with all the prescriptions dispensed during the month. Drugs used each month are recorded from the prescriptions and, when added to the inventory on hand at the end of the month, they must balance with the amounts ordered at the beginning and the inventory at the beginning of the month. Since nothing leaves the pharmacies except upon a written prescription, such a system is possible.

7. Department for shipment of supplies to branch pharmacies:
Lic. Montero in collaboration with the medical staff has published a formulary for use in the Seguro Social hospitals and dispensaries. A section of data of interest to doctors has been included at the end. In the formulary is published a list of

1

2

3

4

SAN JUAN DE DIOS HOSPITAL, SAN JOSE

1. Staff Entrance

2. Dispensing Section of the Pharmacy. Chief Pharmacist Elsa Maria Perez is in the foreground.

3. Outpatient Entrance.

4. Laboratory for the Manufacture of Injectibles.

the regulations governing the prescribing of medications. One of the rules states that if a doctor prescribes a preparation not listed in the formulary, the pharmacist will fill it in order not to delay the treatment of the patient. However, the pharmacy will inform the Director or Sub-Director of Medical Services of the prescription and its cost. Each month the Director of Medical Services will report all these prescriptions and their cost to the auditor, who will in turn report them to the directors of the Seguro Social system.

Purchasing of Supplies in Government

Purchasing of supplies for the department of Pharmacy of the Ministry of Public Health, for the hospitals under the Ministry, and for the Seguro Social Pharmacy follows the usual pattern of government buying with notices being published in the official daily paper, the Gazette, and the lowest bid being accepted. The pharmacist may, however, specify a trade name when ordering.

Private Hospitals

The private hospitals and clinics in the country are as follows: Hospital Clinica-Biblica (sponsored by the Latin American Mission Board), San José; Clinica Mater, San José; Clinica Dr. Montes de Oca, San José; and three United Fruit Company Hospitals. The first three each have a capacity of 40 beds or less and do not employ pharmacists. They send their prescriptions to the nearest drug store to be filled. The United Fruit Company Hospitals have a total of 511 beds and have 6 pharmacists.

United Fruit Company Hospitals.

The United Fruit Company has three hospitals in Costa Rica—one at Limon (213 beds), one at Quepos (88 beds), and one at Golfito (210 beds). The total number of persons employed by the company in Costa Rica is about 20,000. However, the number of people served by the hospital pharmacies is much more than that when the families of the employees are included.

According to the terms of the labor contract, each employee has deducted 2 percent of his wages monthly for which he receives medical care in the hospitals and dispensaries of the company while employed by the company. Families of workers earning up to 500 colones per month are also covered by this deduction, while those earning over this amount must pay the cost of medical care plus 10 percent for their families. The employee on sick leave receives half salary for a period commensurate with the length of time he has been employed. After 3 months of employment he is eligible for one month of sick leave pay, after 6 months of employment he may receive two months of sick leave pay, and after 9 months of employment he may be given sick leave pay for three months.

There is no centralization in the administration of the three hospitals, each one acting independently of the others. All of the hospitals, however, order all drugs and supplies through Maretrop, the purchasing organization for United Fruit Company in New York.

The first licensed pharmacist was employed in the hospital at Limon in about 1928. At present there are two pharmacists in each of the three hospitals.

All of the hospitals have more or less the same formulary, which is a list of the special formulas manufactured in the pharmacies for use in the hospitals and dispensaries. The medical staff is not, however, restricted to a formulary in the sense of a list of the drugs stocked in the pharmacy. Whenever a new drug becomes available, any doctor may request that the pharmacy stock it, whereupon the pharmacist will order it through Maretrop in New York or by air from San José if it is needed immediately. There is excellent cooperation between pharmacist and physician in avoiding duplication, however.

Each of the three hospital pharmacies is responsible for supplying the dispensaries in the surrounding areas. The hospital at Limon services 7 dispensaries, Quepos has 14 dispensaries, while Golfito supplies 20. These dispensaries, with a few exceptions, are staffed by practical persons and are mainly stocked with first aid items as the injured and sick are immediately transported to the hospital. Supplies are delivered to the dispensaries twice a month, or more often, if necessary.

Hospital Pharmacy at Golfito.

Golfito is one of the United Fruit Company's developments on the Pacific side near the Panamanian border. In 15 years there has been a change from jungle waste to an area of productivity which gives employment to 11,560 persons and provides housing for them and their families.

The present hospital at Golfito was built in 1941. There was a small hospital at Palmar in 1938 while construction was going on in the development of the area. Although the number of employees is 11,560, the number of persons actually served by the hospital pharmacy is 22,800.

The two pharmacists work 8 hours a day every day except Sunday. On Sunday they usually work half a day. There are five assistants to the pharmacists.

The pharmacy at the hospital in Golfito is divided into three sections:

1. Main pharmacy.

Here all the manufacturing is done and all prescriptions and stock supplies for the hospital are prepared. The only solution for injection that is prepared is that of morphine.

2. Outpatient dispensary.

Here previously packaged and bottled medications are labeled and dispensed. Anything that must be compounded is taken to the main pharmacy to be prepared.

3. Department for the shipment of supplies to the dispensaries.

The pharmacy reserve stock is kept in the hospital storeroom. There is no pharmacy storeroom.

The number of prescriptions filled per day in the outpatient dispensary is about 100. The number of prescriptions filled in the pharmacy for the hospitalized patients is very small as there is a complete stock of medicines on each ward. The nurses on each ward dispense the medications when ordered by the doctors. Only those prescriptions that must be compounded are sent to the pharmacy. Since there are nurses on duty in all wards 24 hours a day, drugs can be given to the patients without delay.

Conclusion

The daily routine in all types of hospital pharmacies in Costa Rica is more or less like that in the United States. One difference is that the method of dispensing powdered medications in papers is more common in Costa Rica. Another difference is that, except for the United Fruit Company hospitals there are practically no stock supplies of drugs on the wards. Also, there is a great deal of manufacturing done in Costa Rica. Since the cost of imported specialities is quite high, as much as possible the hospital pharmacists compound similar products which the medical staff prescribes instead. In Costa Rica hospital pharmacy has developed in an efficient manner suited to the particular needs of the community.

REFERENCES

1. Peña Chavarría, Dr. A.: *El Formularia del Hospital,* Revista Medica de Costa Rica, (August) 1950.
2. Montero, Lic. R.: *Formulario de las Prestaciones Medicas,* Caja Costarricense de Seguro Social, 3rd ed., 1953.

SEGURO SOCIAL HOSPITAL, SAN JOSE

1. *Seguro Social Hospital*
2. *Storeroom of the Central Pharmacy. The Storeroom Clerk is seated at the Desk beside the Perpetual Inventory Card File.*
3. *Dispensing Section of the Central Pharmacy. Chief Pharmacist Montero is third from left.*
4. *Manufacturing Laboratory of the Central Pharmacy. Chief Pharmacist is to the right.*

The Formulation of a Paraldehyde Suppository

by HAROLD SHEINAUS *and* G. J. SPERANDIO

PARALDEHYDE WAS INTRODUCED into medicine as a hypnotic by Cevello in 1882, and is one of the best and least toxic of hypnotics.[1] It is absorbed rapidly from the gastrointestinal tract and is noninjurious to mucous membranes.[2] Because of its odor and taste, however, it is seldom employed for sedation in ambulatory cases, although it deserves a wider popularity than it has at present. Paraldehyde has also been given rectally for obstetrical analgesia and amnesia,[1] and in cases of delirium tremens.[3] Doses in obstetrical analgesia are rather high, Kane *et al*[2] reporting the use of 1.2 cc. per ten pounds of body weight, and as a basal anesthetic in preoperative anesthesia it is used in amounts of about 15 - 30 cc.[4]

Several requests for this drug in suitable suppositories have been received, and this paper reports the result of our attempts at formulating such a product.

The dosage range of paraldehyde requires that, for rectal administration a large proportion of paraldehyde be incorporated with a minimum amount of vehicle, since the limiting size of a rectal suppository is in the neighborhood of 2 to 3 Gm.

The base used, therefore, should be of sufficiently high melting point to give a solid when admixed with a proportion of paraldehyde. In order to fulfill the condition of sufficient dosage in a usable suppository, it was decided to limit the vehicle to approximately twenty five percent of the total suppository weight. In the experimental work, attempts were made to find the minimum quantity of base which would form a suitable suppository mass with 10 cc. of paraldehyde.

HAROLD SHEINAUS is a Graduate Student in Pharmacy and G. J. SPERANDIO is an Assistant Professor of Pharmacy, both at Purdue University, Lafayette, Ind.

Experimental

A number of oily or fatty materials of relatively high melting points were tried, with unsatisfactory results. Among the substances tried were monostearin, spermaceti, cetyl alcohol, ozokerite, polyethylene glycol 400 monostearate, carnauba wax, and stearic acid. The materials were mixed with varying amounts of paraldehyde but upon cooling either did not solidify satisfactorily, or resulted in a bleeding out of the paraldehyde.

Certain water-soluble substances were incorporated with the materials mentioned above and attempts were made utilizing Tween 61, G-1725 (Atlas), carboxy methyl cellulose, gelatin, pectin, Pluronic F-68, and Carbowax 6000. Of these, only Pluronic F-68 and Carbowax 6000 gave satisfactory results, the latter being the better of the two. The other substances either were not miscible with paraldehyde, or did not solidify satisfactorily.

Further trials were made, using Carbowax 6000 and small amounts of other materials such as kaolin, starch, pectin, CMC, Pluronic F-68, polyvinyl alcohol, cetyl alcohol, and several others, including some of the original fatty substances tried. These additions were detrimental to the finished product in all cases, most of the formulations resulting in too soft a mass.

At this point, it was decided that Carbowax 6000, used alone, was the best vehicle. Trials with various percentages indicated that a formulation consisting of 25 percent Carbowax 6000 and 75 percent paraldehyde would be the best compromise between maximum paraldehyde content and satisfactory hardening.

The following formula and procedure is suggested:

Carbowax 6000	25.0 Gm.
Paraldehyde	75.0 cc.

Melt 25 Gm. of Carbowax 6000 in a suitable vessel over a water bath, and bring to about 70° C. Remove from bath, and add 15 cc. of paraldehyde, mixing thoroughly and rapidly until homogeneous. Add remainder of paraldehyde (60 cc.), mixing thoroughly and rapidly. Chill immediately to a temperature of approximately 35° C., and pour into suitable molds. Chill for 20 minutes before ejecting. The resulting suppositories are smooth, white, and lustrous. Seal immediately in cellophane and store in a cool place.

Since paraldehyde is quite volatile, it is suggested that precautions be taken to minimize its loss by using a closed vessel during preparation. The mold size is left to the discretion of the compounder, depending on the dosage desired. Mold lubrication is unnecessary. The melting point of the product is 29° to 31° C.

Stability

a. Initial checks on loss of paraldehyde by volatilization when suppositories were exposed to air (25° plus or minus 2° C.) showed the following results:

Average initial weight of suppository	2.04 Gm.
Average weight after 24 hour exposure	1.83 Gm.

b. Tin foil wrapping by hand was inadequate protection against volatilization, as can be seen from these results:

Average initial weight, foil wrapped	2.22 Gm.
Average weight after 72 hours	2.16 Gm.
Average weight after 7 days	2.07 Gm.

c. Foil wrapping, plus coating by quick dipping into melted paraffin at 65° C. was somewhat better, giving the following degree of stability:

Average initial weight, wrapped and coated	2.43 Gm.
Average weight after 13 days	2.41 Gm.
Average weight after 27 days	2.39 Gm.

The disadvantages of this method, however, were threefold: first, the finished product did not present a good appearance; second, the finished product was difficult to unwrap; and third, the unwrapped suppository presented a poor appearance due to the marring of its surface by the heat.

d. Further attempts at cold coating with a methyl cellulose gel, and with a polyvinyl alcohol gel, were not satisfactory. Various Carbowax mixtures were also tried, but being soluble in the Carbowax, the paraldehyde apparently leached through.

e. The most satisfactory method tried was one in which the suppositories were hermetically sealed in cellophane:

Average initial weight of sealed suppository	2.21 Gm.
Average weight after 3 days	2.19 Gm.

With proper sealing equipment, this loss can be still further minimized or prevented entirely. This method also has the advantage of good appearance, easy handling and readiness for usage, and quicker release of the medication than from a coated suppository.

Dissolving Time

The suggested formulation gave the following results, when a suppository was dropped into water at 37° C:

Average time for complete dissolution, no agitation	110 sec.
Average time for complete dissolution, gentle agitation	52 sec.

In each case, the paraldehyde was completely released. There was apparently no decomposition at all, based on odor tests. No acetic odor, indicating depolymerization to acetaldehyde, was present.

Discussion

In this formulation, Carbowax 6000 is ideally suited for the base. It is chemically stable, physiologically inert, does not turn rancid[5] and does not enter into combination with the paraldehyde.

Its solubility favors rapid and complete absorption, whereas fatty substances may inhibit absorption by covering the mucous membrane with a hydrophobic layer.

Toxicology studies[6] have shown the polyethylene glycols to be non-toxic and non-irritating to mucous membranes.

Summary

1. A formulation for paraldehyde in suppository form has been presented.

2. A method for increased stability by sealing is suggested.

3. These suppositories are non-toxic and non-irritating when given in proper dosage. They are rapidly-dissolving and constitute a ready and easily administered dosage form when oral administration is not deemed advisable.

REFERENCES

1. Goodman, L. and Gilman, A.: *Pharmacological Basis of Therapeutics,* The Macmillan Co., New York, N. Y., 1941, pages 178-180.

2. Kane, H. S., *et al*: Combined Paraldehyde-Benzyl Alcohol Pain Relief in Obstetrics, *Current Researches in Anesthesia and Analgesia 16*:121 (May-June) 1937.

3. Osol, A. and Farrar, G. E., *et al*: *The Dispensatory of the United States of America,* J. B. Lippincott, Philadelphia, Pa., 24th ed., 1950, page 822.

4. The Pharmaceutical Society of Great Britain: *British Pharmaceutical Codex,* The Pharmaceutical Press, London, 1949, page 648.

5. Gillham, R. W. and Tomlinson, J. E.: A New Suppository Base, Soluble in Water, *Pharm. J.* (London) *162*:472 (June 25) 1949.

6. Smyth, H. F., Jr., *et al*: The Toxicology of Polyethylene Glycols, *J. Am. Pharm. Assoc., Sci. Ed. 39*: 349 (June) 1950.

Developed by American College of Apothecaries

Public Education Program for Pharmacy

THE AMERICAN COLLEGE OF APOTHECARIES recently inaugurated a public health program for pharmacy designed to promote a better appreciation of the profession's contributions to public health. The material to be covered in mailings to about 1500 pharmacists will include such subjects as the cost of medicines, life expectancy, conquest of killer diseases, educational requirements for pharmacy, self-medication, and many others.

This monthly service available from the American College of Apothecaries provides (at a cost of $6.00 monthly) 1,000 prescription inserts, 100 mailing stuffers, 1 counter card, 1 article, and miscellaneous other material, all pertaining to the subject for that month.

The Cost of Medicines

The first subject to be covered in this public health education program for pharmacy is the cost of medicines. If everything is taken into account, the cost of medicine today is less expensive than ever before. The medical treatment obtainable in this country cannot be purchased for any price elsewhere in the world today.

Although the initial cost of a prescription may often seem high the over-all total cost, when related to the results obtained, represents a great bargain. Twenty years ago a case of lumbar pneumonia cost a patient $1,000 in hospital, nursing, and medical bills, plus an extended loss of wages. In addition, 28 persons out of every 100 died. Today a short series of treatments with antibiotics will eliminate pneumonia in about one week with an over-all cost of much less than $200.

The dollar spent for medical care today is purchasing much more than could ever possibly be conceived 15 years ago.

Life Expectancy

A second topic to be covered by the American College of Apothecaries in this educational program is that of life expectancy.

Many factors have contributed to the longevity of today's population and the increase in life expectancy of the adult of tomorrow. Improved nutrition, education, living facilities, as well as medical advances, have all been partially responsible. One of the most dominant factors has been the development of new and effective pharmaceutical products and their widespread, intelligent use by the medical profession. Pharmacy's contribution in providing effective medication for controlling diseases among children and reducing the death rate constitute one of the brightest chapters in the history of public health. The medical and pharmaceutical professions may be justifiably proud of the contributions they have made.

These are but two of the many subjects the American College of Apothecaries will cover in the program to educate the public concerning pharmacy's role in health. Further information regarding pharmacists' participation in this campaign may be obtained from the American College of Apothecaries, Robert E. Abrams, Secretary, 2173 Knorr Street, Philadelphia 49, Pennsylvania.

CURRENT LITERATURE

edited by SISTER MARY ETHELDREDA, *St. Mary's Hospital, Brooklyn, N.Y.*

American Professional Pharmacist

NOVEMBER, 1953—"A Comment on Mental Hospitals," by George I. Freedman, Chief, Pharmacy Services, Veterans Administration Hospital, Bedford, Mass. Describes the general and special services necessary in such an institution. *page 918*

DECEMBER, 1953—"It is Time for Pharmacy to Start Specializing," by Charles H. Becker, Associate Professor of Pharmacy, University of Florida. The author presents his views on the subject of curriculum and the requirements which are necessary to adequately train pharmacists. Includes suggested courses and credit hours in hospital pharmacy. *page 992*

"Recognizing Matters of Policy," by John J. Zugich, B.Sc., M.P.H. A complete and comprehensive presentation of making policy for the hospital pharmacy *page 1006*

Hospital Management

NOVEMBER, 1953—"How Prepackaging Saves Time, Money," by Edward Superstine, Assistant Chief, Pharmacist, Duke Hospital. Describes methods of prepackaging and coding for identification of items for both inpatient and outpatient departments. *page 83*

DECEMBER, 1953—"BIGGEST — Little Department" by Eli Fish. Describes the physical setup and the operation of the pharmacy at the new North Shore Hospital, on Long Island, N.Y.

Hospitals

DECEMBER, 1953—"Preparing the Hospital Budget"—A special feature. Presents the factors considered in anticipating a budget and the numerous points important in its preparation. Pharmacy Department is included. *page 69*

JANUARY, 1954—"A Narcotic Control System for the General Hospital," by George F. Archambault, D.Sc., LL.B. Describes the accurate check of the use and inventory of narcotics at the pharmacy and nursing stations as developed in the U. S. Public Health Service hospitals. *page 112*

Hospital Progress

NOVEMBER, 1953—"The Control of Drugs," by Irvin Kerlan, M.D. The second portion of a two-part article which first appeared in the October issue. Presents the type of violations against the Food, Drug and Cosmetic Act which the Food and Drug Administration attempts to curb. *page 69*

DECEMBER, 1953—"Road to Maturity: The Philosophy of Pharmacy Operation," by Ann Langley Czerwinski. The ideals and ethical values of pharmacy operation based on a spiritual philosophy are here presented. *page 64*

The Hospital Pharmacist (Canada)

NOVEMBER-DECEMBER, 1953—"Narcotics in Solution." A documented summary of the advantages of using narcotics in solution rather than the hypodermic tablets. *page 328*

J. Am. Pharm. Assoc., Pract. Pharm. Ed.

NOVEMBER, 1953—"Pharmaceutical Vehicles: A Study of Their *p*H and Incompatibilities," by Clifford W. Riegler, Jr. and J. Leon Lichtin. Results of compatibility tests using a number of the common vehicles were reported. Incompatibilities of Sodium Phenobarbital with various vehicles are given. *page 706*

DECEMBER, 1953—"The Use of Aqueous Elixir in Modern Drug Formulation" by H. D. Fifer and S. J. Dean. A formula for a modified aqueous elixir is suggested as a vehicle for stable preparations. According to the study, the vehicle is superior to syrups in cutting down the unpleasant taste and subsequent aftertaste of the succinates. *page 771*

Modern Hospital

DECEMBER, 1953—"The Hospital That Faith Built," by George J. Maguolo. Describes and presents the floor plans of the selected "Modern Hospital of the Month." Plan of hospital pharmacy included. *page 65*

"Rodenticides" by Carl C. Pfeifer, M.D. A summary of rodenticides in use today. Includes antidotes for accidental poisoning. *page 108*

Southern Hospitals

DECEMBER, 1953—"The Formulary System: Progressive or Socialistic," by Jane L. Rogan. A realistic presentation of the use of the formulary system and its advantages to patient, medical staff, pharmacy and hospital. *page 67*

therapeutic TRENDS

edited by LEO F. GODLEY

6—Mercaptopurine in Leukemia

Burchenal *et al,* working at Sloan-Kettering Institute in New York, reported on the use of the antimetabolite, 6-Mercaptopurine (6MP) in *Blood 8*:965 (Nov.) 1953.

This drug was used on a series of 107 patients with neoplastic diseases. It was administered orally in 50 mg. tablets. The average tolerated dose was 2.5 mg/Kg./day. The plan in this study was to give the maximum tolerated dose unless therapeutic response occurred before the beginning of the symptoms of toxicity. Hospital patients had daily leukocyte counts and hemoglobin determinations; platelet and reticulocyte counts were done weekly. Outpatients had blood counts once or twice weekly.

The most significant side effect was a depression of bone marrow; and in excessive doses, it produced leukopenia, anemia, thrombocytopenia and bleeding. Nausea and vomiting were rare.

There were 45 children in this series with acute leukemia; all except 14 experienced some degree of benefit after treatment with 6 MP. Of the 12 adults with acute leukemia, 4 obtained some clinical hematological improvement.

Patients having other types of malignant processes were treated without significant benefit. There is some evidence that it may be of benefit in chronic myelogenous leukemia. It appears from the above results that children with acute leukemia were the most benefitted. Burroughs Wellcome will market this antimetabolite under the tradename, "Purinethol."

Oral Procaine for Heartburn

Oren, in Miami's Jackson Memorial and Mount Sinai Hospitals, conducted a study in which procaine was administered orally to 38 patients who have had heartburn as a chief complaint for long periods of time. A teaspoonful of two percent solution of procaine hydrochloride along with a teaspoonful of Metamucil was given with water 15 minutes before meals. Treatment also included a bland diet and an anti-spasmodic-sedative medication.

Complete symptomatic relief was experienced in 18 patients, partial relief in 6 and there was no relief or aggravation of symptoms experienced by 14.

It was determined that procaine was contraindicated or had no beneficial effect on peptic ulcer; 80 mg. of procaine has a stimulating effect upon acid secretion in the stomach similar to that produced by 50 cc. of seven percent alcohol. It was further determined that procaine may possibly relieve spasm temporarily by direct action on smooth muscle of the gut. This study was published in *Southern Med. J. 46*:946 (Oct.) 1953.

Benadryl for Post Operative Nausea

Benadryl in 100 mg. intravenous doses was given to 180 patients to prevent and/or control postoperative nausea and vomiting. The results obtained in this study and published in *Surgery 34*: 837 (Nov.) 1953 are gratifying to the extent that these investigators indicate that it might be adopted as a routine procedure.

The authors point out that the intravenous route is preferable and that doses under 50 mg. were not reliable. The usual side effects of Benadryl are sometimes noted; but the drug in no way impaired the course of anesthesia or post operative recovery of the patient.

Ophthaine, an Anesthetic for the Eye

Ophthaine, Squibb (2-diethylaminoethyl 3-amino-4-propoxybenzoate hydrochloride) is an amorphorus, whitish chemical. It forms clear solutions with water and dilute acids; but is incompatible with alkalis.

Boozan and Cohen reporting in *Am. J. Ophth. 36*: 1619 (Nov.) 1953 show that in the extended period of clinical trial and observation in New

York University Bellevue Medical Center, this drug was found to be a safe and potent anesthetic agent for all ophthalmological procedures.

Ophthaine was used in 0.25 to 0.5 percent concentration in normal saline preserved with chlorobutanol. In 43 surgical ophthalmological operations, a level of anesthesia was attained to permit any desired surgical manipulation.

In comparison with Tetracaine Hydrochloride 0.5 percent Solution and Ophthaine Hydrochloride 0.5 percent Solution, a series of subjects were given one drop of Ophthaine in the left eye and one drop of Tetracaine in the right eye. Time of onset of anesthesia, duration of anesthesia, and degree of conjunctival hyperemia were essentially equal for both drugs. There were no local or systemic toxic effects noted; but pain on instillation was considerably less with the Ophthaine solution. This, apparently, as far as these investigators are concerned, is of great importance particularly since is is a point that is directly reflected in the comfort of the patient.

Cellulose Sponges in Surgery

Sponges manufactured from cellulose recovered from wood instead of ordinary gauze sponges have been used in a variety of surgical procedures at Buffalo General Hospital. These sponges were manufactured by O-Cel-O Division of General Mills, Inc. In the preparation of this product the cellulose is dissolved in sodium hydrochloride and carbon disulfate. In the liquid stage, particles of barium sulfate are incorporated to provide radiopaqueness. The material is extruded through a special orifice to produce certain physical characteristics. The sponges that were used in this study were 4″ x 8″ and 1 mm. thick. The absorbent quality is approximately twice that of the ordinary gauze sponge; and the wetting and absorption speed are far superior to cotton.

These cellulose sponges can be rinsed and reused repeatedly during the same operation requiring considerably fewer sponges, hence, the cost is less and the ease of maintaining the sponge count is appreciated by the nursing staff. The material is nonsensitizing; but there are certain deep and narrow incisions that cannot be reached by the sponge in present use. These clinicians point out in *Surgery 34*:803 (Nov.) 1953 that gauze sponges are still a necessity and that both types find a definite place in surgery.

Serum Albumin in Barbiturate Poisoning

After treatment with analeptic drugs failed, 25 percent Serum Albumin (salt poor, human) was used to advantage on three patients who were severely toxic due to barbiturate poisoning. This was reported by Mousel in *J. Am. Med. Assoc. 153* :459 (Oct. 3) 1953.

The presumed rationale for this treatment was that the symptoms elicited were due to cerebral edema which was corrected by the osmotic effect of the serum albumin. Reflexes returned to the three patients in this study in 23, 8, and 17 hours respectively after administration of the serum albumin. After the appearance of reflexes, there was a gradual and uneventful return to normal status and there were no maniacal tendencies evident or restraints necessary.

Prenderol in Petit Mal Epilepsy

Prenderol, Squibb (2,2-diethyl-1,3 propanediol) has skeletal muscle relaxing properties and has been used heretofore in situations similar to mephenesin.

Perlstein, at Cook County Hospital in Chicago, reported his study on 103 patients in *Neurology 3* :744 (Oct.) 1953 wherein he states that Prenderol is one of the three most effective tools in the management of petit mal epilepsy. It appears that Prenderol is more effective than Paradione but less effective than Tridione. It is, however, less toxic than Tridione and it would appear to be the drug to try first in the management of petit mal.

Prenderol is absorbed and excreted so rapidly that it would have to be given every one or two hours to maintain an effective therapeutic concentration; however, retarders to Prenderol absorption may be used such as cream, butter, olive oil, polyvinyl-pyrrolidone and methyl cellulose.

Piperazine for Pinworms

Piperazine hydrate was considered the drug of choice in combatting oxyuriasis in children. Cure was obtained in all but one of 31 infected patients using this agent. The dose employed was 50 to 75 mg./Kg./day given in a morning and a night dose for 7 days, then a 7 day rest and another 7 day course of medication.

There were no significant side effects. Overdoses produce vomiting. In this study at Guy's Hospital in London, White *et al* found that Gentian Violet produced a 70 percent cure but was undesirable because of nausea and staining. There was a 19 percent spontaneous cure using a placebo. Diphenan was no more effective than the placebo.

This report appeared in *Brit. Med. J. 2*:755 (Oct. 3) 1953. The material was furnished by Wellcome Laboratories. In this country Burroughs Wellcome has an equivalent product under the trade name Antepar.

timely drugs

Achromycin

. . . is a new antibiotic for use in treating a wide range of bacterial and rickettsial infections. Also known as tetracycline, it is related chemically to Aureomycin or chlortetracycline. Achromycin is a product of Lederle Laboratories Division, American Cyanamid Company. Clinical trials reported recently have shown the drug to have fewer side reactions and greater stability than the older related antibiotics. Achromycin also has an increased ability to penetrate body tissues and fluids. It will be used in the treatment of a wide range of infections, such as pneumonia, meningitis, osteomyelitis and others. Achromycin is available for both oral and intravenous use.

Amphedase Kapseals

. . . is a combination of vitamin components—nicotinamide, thiamin hydrochloride and ascorbic acid—along with *dextro*-amphetamine sulfate and Taka-Diastase. Supplied by Parke, Davis and Company, Amphedase Kapseals are indicated in the management of asthenia, convalescence, depression, obesity, faulty nutrition, chronic alcoholism and geriatrics.

Antepar Citrate Syrup

. . . for the treatment of pinworm infestation (enterobiasis, oxyuriasis) and an anthelmintic to *Enterobius vermicularis,* is available from Burroughs Wellcome and Company. It is supplied in the form of a syrup containing the equivalent of 100 mg. of piperazine hexahydrate per cc. (approximately 500 mg. per teaspoonful). Antepar Citrate Syrup is virtually non-toxic in therapeutic doses and is well tolerated.

Bicillimycin All-Purpose

. . . is a compound of five different antibiotics—long acting Bicillin, procaine penicillin, potassium penicillin, streptomycin and dihydrostreptomycin. For use in the treatment of mixed or multiple infections, or as a prophylaxis prior to surgery, the compound has proved valuable in the treatment of peritonitis and urinary tract infections. Bicillimycin All-Purpose is administered by deep intramuscular injection and is supplied in single dose vials of dry powder, stable for two years at normal temperatures. Sterile distilled water is added as a diluent to make a total volume of 3 cc. prior to injection. It is available from Wyeth Laboratories.

Coricidin Pediatric Medilets

. . . is a combination of the antihistamine, Chlor-Trimeton maleate, aspirin and acetophenetidin. Available from The Schering Corporation, the preparation is especially recommended for children in the relief of nasal symptoms of colds and aches and pains accompanying a cold. Coricidin Pediatric Medilets are supplied as multi-colored, candy-like tablets with a cherry aroma and flavor.

Coricidin with Penicillin G Procaine

. . . is a combination of Chlor-Trimeton Maleate, penicillin G procaine, aspirin, acetophenetidin and caffeine. It is available from the Schering Corporation. Coricidin with Penicillin G Procaine is indicated in the treatment of acute upper respiratory infection, which is frequently complicated by secondary bacterial infection. The oral penicillin also has been effective prophylactically in studies on the prevention of the recurrences of rheumatic fever. The usual adult dosage is 4 to 6 tablets daily, taken one hour before or two hours after meals.

Cortril Ophthalmic Ointment

. . . is a preparation of hydrocortisone acetate available from Pfizer Laboratories. It is for use in the local treatment of allergic, bacterial and traumatic eye inflammations. Cortril Ophthalmic Ointment is available in one-eighth ounce tubes at strengths of 0.5 percent and 2.5 percent.

Cortril Topical Ointment

. . . for the treatment of allergic dermatoses, is a hydrocortisone acetate preparation. Supplied by Pfizer Laboratories, Cortril Topical Ointment is available in strengths of 1.0 percent and 2.5 percent.

Diamox

. . . is a non-mercurial diuretic for patients suffering from congestive heart failure. It increases the output of salt and water from the kidneys even when the heart is weakened. Diamox has been placed on the market by Lederle Laboratortories Division, American Cyanamid Company.

Erythrocin with Sulfas

. . . is a combination of erythromycin stearate sulfadiazine (as sodium salt), sulfamerazine (as sodium salt), and sulfamethazine with aluminum hydroxide as a buffer. Supplied by Abbott Laborator-

ies, Erythrocin with Sulfas is contained in a new "Film Seal" tablet, rather than an enteric coating. This facilitates swallowing and seals in the taste of the drug. The special buffer protects the Erythrocin Stearate from gastric secretions and makes for swift absorption of the drug in the upper intestinal tract.

Erythrocin with Sulfas is indicated in infections caused by staphylococci, streptococci and pneumococci, especially in patients allergically sensitive to other antibiotics or where the organism is resistant. This preparation should be reserved for infections in which the sensitivity of the organism to the combination has been shown to be greater than to Erythrocin alone. Erythrocin with Sulfas may also be indicated in mixed infections, especially of the respiratory or urinary tract.

Erythroguent

. . . is an ointment containing the antibiotic erythromycin 5 mg. per gram, with methylparaben 0.2 mg. and butyl-*p*-hydroxybenzoate 1.8 mg. It is useful in the treatment of various cutaneous bacterial infections, producing prompt response in such conditions as impetigo, impetiginous dermatitis, folliculitis, paronychia, external otitis, secondarily infected eczema, burns and ulcers. Erythroguent may be applied two to five times daily and in severe or extensive infections, local therapy should be supplemented with erythromycin and/or sulfonamides by mouth or penicillin by injection. It is available from The Upjohn Company.

Furacin Urethral Suppositories

. . . containing Furacin, brand of nitrofurazone, and diperodon hydrochloride dissolved in a water-dispersible base composed of glyceryl monolaurate and sorethytan monostearate are available from Eaton Laboratories. Furacin Urethral Suppositories are indicated in non-gonorrheal, bacterial (granular) urethritis in women.

Gantricillin (acetyl)-200

. . . provides a preparation containing both Gantrisin and penicillin and having a potent action against a wide range of gram-positive and gram-negative micro-organisms. It is especially recommended for infections in which the causative agents are more susceptible to combined antibacterial therapy than to either penicillin or Gantrisin alone. A product of Hoffmann-La Roche, Gantricillin (acetyl)-200 is a cherry-flavored suspension especially useful for children. Each 5 cc. of the preparation contains 200,000 units of penicillin G potassium plus 0.5 Gm. of Gantrisin, the highly soluble, wide-spectrum, single sulfonamide, in the form of Gantrisin (acetyl).

Marezine Hydrochloride

. . . brand of cyclizine hydrochloride, is an antiemetic indicated for motion sickness. The product is supplied by Burroughs Wellcome and Company in 50 mg. scored tablets.

Penicillin-PBZ Tablets

. . . is a combination of penicillin and Pyribenzamine supplied by Ciba Pharmaceutical Products, Inc. Tablets are available in two dosage sizes—one containing 200,000 units of penicillin and 50 mg. of Pyribenzamine and the other tablet containing 200,000 units of penicillin and 25 mg of Pyribenzamine. Penicillin-PBZ Tablets are used to minimize or prevent sensitivity reactions to penicillin through the use of an oral dose whenever penicillin is prescribed by the physician. Dosage varies with the individual case, and should be used as prescribed by the physician.

Readicillin

. . . is a palatable, cherry-flavored, red-colored suspension of penicillin G potassium in vegetable oil available from The Upjohn Company. Each 5 cc. of the suspension contains 300,000 units of penicillin G. Indications for using Readicillin are the same as for other forms of oral penicillin. These include staphylococcic, streptococcic and pneumococcic infections, Vincent's stomatitis, and gonorrhea. Readicillin provides high initial blood levels of penicillin (0.65 unit per cc. in one hour) and detectable levels are present for eight hours in most patients. It is particularly useful in pediatrics, but may be preferred by many adults. The recommended dosage is one teaspoonful orally every eight hours. In more severe infections, two teaspoonfuls every eight hours may be used.

Syrasulfas

. . . is a suspension of the three sulfonamides, sulfadiazine, sulfamerazine and sulfamethazine, 0.167 Gm. of each per teaspoonful of the syrup. Syrasulfas is used in the treatment of infections caused by organisms susceptible to the sulfonamides—such as pneumococcic, streptococcic staphylococcic, and meningococcic infections. The incidence of crystalluria or renal damage is minimized by the use of the three sulfonamides. The recommended dosage for adults is 6 to 8 teaspoonfuls initially, followed by two teaspoonfuls every six hours. For children (25 to 100 pounds), the dosage is 2 to 6 teaspoonfuls initially, followed by 1 or 2 teaspoonfuls every six hours. Syrasulfas Syrup is a product of The Upjohn Company.

Thytropar

. . . is a highly purified thyrotropic principle of bovine anterior pituitary glands indicated for use as follows:

1. To help differentiate primary thyroid myxedema from that due to pituitary insufficiency.

2. To intensify the effect of iodine-131 in the treatment of functional thyroid malignancy.

3. To shorten the course of acute thyroiditis.

If pituitary myxedema is suspected, Thytropar should be administered as cautiously as thyroid extract, to avoid precipitating adrenocortical insufficiency.

Thytropar is supplied by The Armour Laboratories as a sterile, lyophilized powder in 6 cc. vials. containing ten U.S.P. Units of thyrotropic activity per vial, each unit representing the potency of twenty milligrams of the tableted preparation of the U.S.P. reference substance. It is stable indefinitely at room temperature while in the dry state. Thytropar dissolves readily in physiologic salt solution and retains its potency in solution for at least four days, if refrigerated.

Vi-Dexemin

. . . is a new product designed for the control of weight during pregnancy. Introduced by Smith, Kline and French Laboratories, Vi-Dexemin contains *dextro*-amphetamine sulfate plus protective amounts of essential vitamins and minerals.

Readers are encouraged to submit their production problems or describe unusual and unique equipment items which they have found useful

EQUIPMENT TOPICS

by PAUL F. PARKER AND CLIFTON LATIOLAIS

One of the real pleasures for hospital pharmacists is the opportunity to exchange ideas concerning equipment or production problems. Equipment planning needs, however, should be approached from a well defined, systematic viewpoint. Such an approach should answer the questions why and how. It is usually assumed that a hospital pharmacy manufacturing program is established to provide increased economy, to furnish pharmaceutical products which are not commercially available, or for teaching purposes. If such is the case, then an attempt should be made to assign a relative value of each purpose to the cost of establishing and operating a manufacturing program. Secondly, consideration should be given to the quality, quantity and production scheduling for each item or group of items to be manufactured. Not unusually, one piece of equipment may be used in multiple operations. This not only justifies the original cost of the equipment, but also utilizes the machinery at more nearly its maximum capacity. It then becomes necessary to continuously develop production plans and integrate them with newer items of equipment which meet these needs.

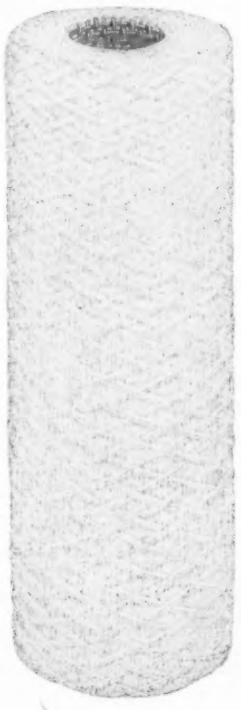
To establish or expand a small scale manufacturing program, the equipment problems can most often be answered in one of three ways: (1) by individual ingenuity together with a well equipped machine shop to make the necessary piece of equipment, (2) by adapting equipment which is commonly used in the food, chemical, paint, pharmaceutical, and other industries or, (3) by the purchase of equipment which is suitable in size to the production required. The purpose of this column is to bring to the attention of the hospital pharmacist some miscellaneous equipment ideas which he may find adaptable to his equipment problems by one or a combination of the above methods.

FILTRATION OF BULK SOLUTIONS

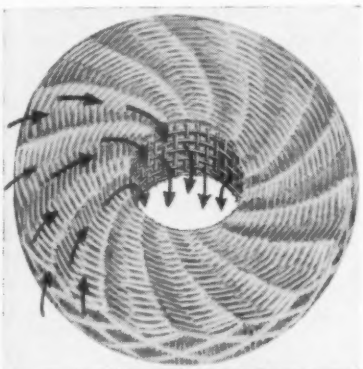
A simple and inexpensive filtration-liquid transfer unit may be made by purchasing a filter apparatus, pump and fittings for mounting as a portable unit in a convenient manner. Many hospital pharmacists who operate a manufacturing program have for several years used an asbestos pad-type filtering mechanism for filtering oral preparations, x-ray and photographic solutions, soaps, germicidal solutions, etc. Such a unit costs at least $500 or more, including the motor and transfer pump. In addition from two to four asbestos pads which cost from twelve to fifteen cents each are usually used for each filtering operation. There is no doubt that this equipment provides a quality filtrate, however, perhaps it would be well to evaluate the quality of filtration necessary in solutions of this type.

A considerably less expensive filtration mechanism may be adapted from a commercially available cone-type filter which is housed in a small metal jacket. The liquid is forced by pump through the cone or tube which is made of various filter media to meet the individual requirements. The cones are available in materials such as cotton cellulose, nylon, orlon, acrylic fiber, dynel, cellulose acetate and glass fiber to fulfill special needs. It is suggested that a specific filter tube be kept for each type of filtering operation. Since the filter cones may be reused over a period of time, they should be stored either in a plastic bag or in individual glass jars of solution and labeled for their respective uses. The metal jackets or cases are also available in various materials such as steel, stainless steel, brass, Monel, nickel and steel with rubber or plastic lining to meet a diversity of operating conditions. The filter case specifications should be made to meet the maximum hazards to be encountered by the various filtrants (probably stainless steel) and the filter cone selected for the problem posed by each filtrant. Fulflo filters are manufactured by the Commercial Filters Corporation, Melrose 76, Mass. The cost of the filter case is approximately $55.00 and the filter tubes cost from $1.00 to $2.00 each, depending upon the type of material selected.

In the manufacture of the filter tubes the fiber is spun into a coarse yarnlike "roving" which is then precision wound into a predeter-



mined pattern on an open metal or plastic core to form a thick walled cylinder traversed radially by a network of diamond shaped passages. As the "roving" is wound, a fine film of fibers is drawn from the "roving" across each diamond tunnel and the free ends of these fibers are locked in place by the next layer of "roving." This locking prevents rupturing, channeling, bypassing and fiber migration.



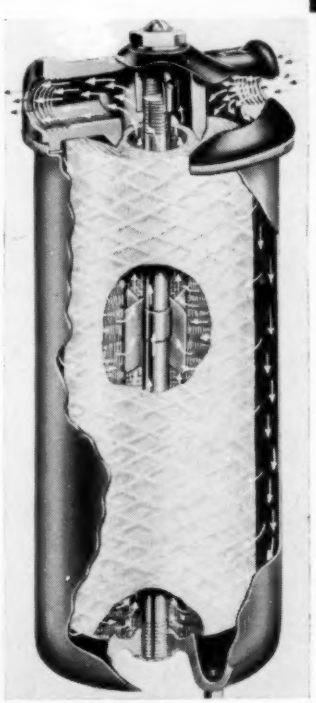
As the fluid passes from the outer surface of the filter tube to its inner core, the fluid stream is subdivided into numerous small streams which must pass through the diamond tunnels where they encounter many successive fine filtering films of gradually increasing density. The spaces between the filtering films constitute cells where separated impurities can accumulate. This prevents the blinding effect of surface loading and assures greater filter tube element life.

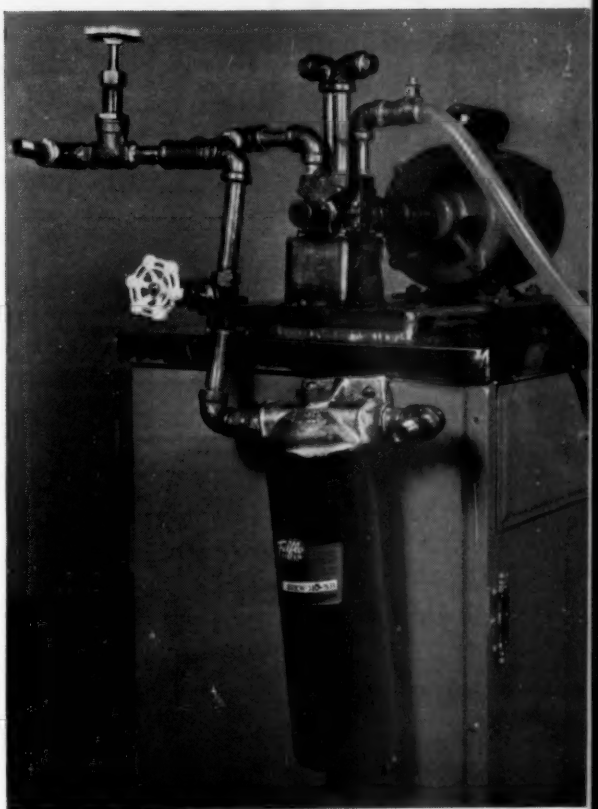
TRANSFER PUMP

The filter and transfer unit may be made complete by the purchase of a small pump and the necessary fittings. The entire unit may be mounted permanently on a table, used bedside stand with casters (see illustration) or some similar type of portable unit.

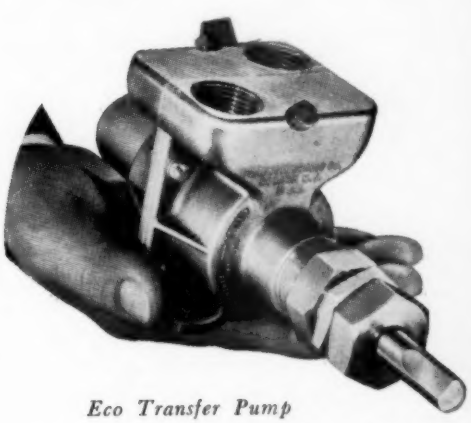
To prevent the transfer of large or small quantities of liquid from becoming a time consuming and uneconomical problem it is necessary to have a mechanical pump which will meet the following requirements: (1) fast flow rate, (2) simplicity of operation, (3) easily cleaned, (4) versatility, (5) compactness and (6) be non-corrosive. The Eco AllChem gearless, stainless steel transfer pump meets most of these requirements. The pumping motion of these pumps is based on two opposed axially oscillating impellers. The impellers are available in rubber, nylon or toflon, the latter being the best. The pumps are available in two sizes with capacities of 3.5 or 10 gallons per minute at 1725 R.P.M. They are positive displacement pumps, hence the rate of delivery is constant, non-pulsating and capacity is directly related to speed. Once filled, the pumps are self priming thereafter. As optional fittings, two extra ports are available, thus giving two suction and two discharge ports.

The Eco pump is manufactured by the Eco Engineering Company, Newark, New Jersey.





Fulflo Filter Unit and Eco Transfer Pump shown mounted on table as a portable unit.



Eco Transfer Pump

The liquid is forced by pump into the jacket through the filter cone into the core of the cone and out through the opposite side of the jacket. The jacket may be obtained in a variety of metals.

Notes and Suggestions

PRACTICAL FORMULAS FOR USE IN HOSPITALS

CALAMINE TABLETS

Tablets of calamine for the preparation of calamine lotion may be made from the following formula:

Veegum*	1.00 Gm.
Calamine	6.80 Gm.
Zinc Oxide	6.80 Gm.
Sodium Carboxymethylcellulose, medium viscosity	0.85 Gm.

These may be dispensed as calamine lotion simply by dispersing them in water and glycerin (water 76.55 cc. and glycerin 3.00 cc.), and finally adding the wetting agent, dioctyl sodium sulfosuccinate 1 percent (5 cc.). This is an extremely easy way of preparing calamine lotion. There is no weighing out of dry powders, and large supplies of tablets can be stored in a small space. This formula appeared in Technical Bulletin No. 122 of the R. T. Vanderbilt Co. Specialties Department.

CALAMINE OINTMENT

The traditional calamine ointment has long been a source of difficulty to pharmacists. The following formula illustrates a smooth, creamy, easily spread calamine ointment. It is easily prepared and ages extremely well.

Veegum*	5.0 Gm.
Polyoxyethylene Stearate	5.0 Gm.
Water	70.0 cc.
Glycerin	5.0 Gm.
Calamine	6.8 Gm.
Zinc Oxide	6.8 Gm.
Phenol, Liquid	0.5 cc.

Add the Veegum to the water slowly, continually agitating until smooth. Add the polyoxyethylene stearate and glycerin, and heat to 50°C. with stirring. Mix until cool. Mix other ingredients together. Add a small amount of Veegum and water mixture to other ingredients already mixed and mull to a paste. Gradually combine remainders and mix mechanically until smooth and uniform. This formula appeared in Technical Bulletin No. 122 of R. T. Vanderbilt Co. Specialties Department.

*Veegum is a complex colloidal magnesium aluminum silicate available from the R. T. Vanderbilt Co., 230 Park Ave., New York 17, N. Y.

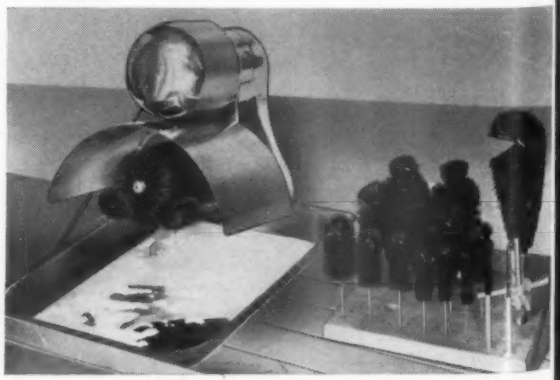
LABORATORY GLASSWARE WASHER

All types, sizes, and shapes of glassware from 10 mm. to 4½" in diameter up to 8¾" in length for wide mouth vessels and 6¾" in length for narrow neck, can be washed with this portable unit.

No soaps or detergents are necessary; the steady revolving of the brushes with constant friction action does the cleaning. Centrifugal force prevents nylon bristles from becoming clogged.

The washer is furnished with a set of interchangeable brushes for the bulk of small and medium sized glassware; a jet rinser is included. The unit is hung above any sink and plugged into a standard 110-volt outlet. No additional plumbing or water connection is required.

The washer, which is 14" wide, 14½" deep and 12" high, weighs 39 pounds, and is available in two models from Scientific Glass Apparatus Company, Inc., Bloomfield, New Jersey. Model W1050X, for capacities up to 1,000 cc., is complete with jet rinser, brush accessories, and ¼ h.p. 110-v, 60-cycle A.C. drip-proof motor, each $220.00. Deluxe Model W1052X is similar but has speed changer for capacities up to 2,000 cc. and is available for $285.00.



RECTAL SUPPOSITORIES AS ENEMAS

The use of rectal suppositories instead of enemas in obstetrics is described by E. A. Banner in the October issue of the *Proceedings of the Staff Meetings of the Mayo Clinic* (p. 567). The composition of the suppositories is as follows:

Sodium Bicarbonate	0.60 Gm.
Potassium Bitartrate	0.90 Gm.
Calcium Silicate	0.05 Gm.
Bentonite U.S.P. XIII	0.30 Gm.
Polyethylene Glycol	0.20 Gm.
Dextran 282	0.05 Gm.
Cocoa Butter	0.05 Gm.
Vegetable Lecithin	0.10 Gm.
Talc	qs

This preparation, when in contact with the rectum, is stated to develop a minimal amount of carbon dioxide gas which, when liberated, has a stimulating influence on the peristaltic and defecation reflexes. Early ambulation is suggested in order to assist this reflex.

No serious side effects have followed administration although some patients experienced minor gas pains. Patients preferred suppositories to enemas and the use of a single suppository was successful in 60 to 65 percent of all patients. If after 30 minutes evacuation was not accomplished, a second suppository was inserted, and this increased the overall efficiency by about 5 percent. The author believes that a rectal suppository acts as a satisfactory substitute for enemas during the postpartum state, thereby increasing the efficiency of nursing personnel, substantially decreasing the cost of overall operation and minimizing discomfort to the patient.

These suppositories are commercially available from Pharmacia Laboratories, Inc., Rochester, Minnesota.

COUMARIN REPLACEMENT

A new flavoring ingredient, Protovanol C, has been developed by the Florasynth Laboratories Inc., New York, to replace coumarin, which it is said to equal in strength. It is claimed to mix readily in various dry bases, to be easily absorbed in cane sugar, corn sugar or starch, and to be completely soluble in alcohol, propylene glycol, and to some extent in vegetable oils.

The use of coumarin in flavoring agents has been discouraged by The Federal Food and Drug Administration because of its possible toxic effects.

NON-SOAPY DETERGENT

Sodium Lauryl Sulfate (Duponol C)	15 Gm.
Distilled Water, to make	100 cc.

TABLET COUNTER

A hand operated, bench type tablet counter is available from the Arthur Colton Co., 3400 E. Lafayette, Detroit 7, Michigan, which has a capacity of about 15 bottles per minute with not more than 100 count, medium size tablets. These are ordered for specific tablet sizes and, although one tray is included with the counter, additional various size trays may be ordered separately.

The model, Colton No. 715, illustrated occupies an area of 14″ x 18″, with a height of 12″, and is priced $115.00 F.O.B. Detroit (subject to 15% educational institution discount).

BUBBLE BATH

Sodium Lauryl Sulfate	35 Gm.
Sodium Sesquicarbonate	63 Gm.
Sodium Alginate N.F.*	2 Gm.
	100 Gm.

Mix the powders; color and perfume to suit.

DRY SCALP DETERGENT

Aerosol OT (100%)	10 Gm.
Olive Oil	90 Gm.
	100 Gm.

Dissolve the Aerosol in the olive oil heated to 70°C. Perfume, if desired.

METAL MARKING INK

Rosin	20 Gm.
Alcohol	150 cc.
Sodium Borate	35 Gm.
Water	250 cc.
Methylene Blue, to tint	

Dissolve the rosin in alcohol and add resulting solution drop by drop to the sodium borate which has been dissolved in the water. Finally, add sufficient methylene blue to obtain the desired tint.

STAIN REMOVER FOR PLASTIC DISHES

Sodium Perborate	20 Gm.
Trisodium Phosphate	80 Gm.

*Available from Algin Corp. of America, 24 State St., New York, N.Y.

ASHP affiliates

Greater New York Chapter

The November 17 meeting of the Greater New York Chapter of the ASHP was held at Mercy Hospital, Rockville Centre, N.Y. Papers presented at the 1953 Institute held in Kansas City were reviewed by Sister Cecelia Mary and Sister Mary Patrick. These covered "Professional and Administrative Policies Governing Pharmacy Services," "Pharmacology of Drugs Acting on the Autonomic Effector Cells," and "Hospital Pharmacy Records."

Michigan Society

Members of the Michigan Society of Hospital Pharmacists met at Harper Hospital in Detroit on November 12. The principal speaker was Dr. A. B. Hill who spoke on skin grafting and other phases of plastic surgery.

North Carolina

Hospital pharmacists in North Carolina met at Alamance County Hospital for an informal meeting on November 19. Mr. Sandy Griffin, Chief Pharmacist, was host to the group. Committee chairmen for the current year include Rudolph Hardy, *Program and Public Relations*; William W. Taylor, *Membership*; Halcyone B. Collier, *Publicity*; Virginia Caudle, *Historian*; Gilbert Colina, *Projects*; and Ernest W. Rollins, *Nominating*.

Florida Society

The annual meeting of the Florida Society of Hospital Pharmacists was held in conjunction with the Florida State Hospital Association Convention in Miami Beach, Fla. December 3, 4 and 5. Mrs. Anna D. Thiel, President, presided over the meeting which included a round table discussion covering hospital forms, floor stocks, emergency medication, government pharmacy, pharmacist - physician relationship, purchasing and internship program. The discussion was moderated by Mr. Charles Haupt, Bureau of Professional Relations, University of Florida College of Pharmacy. Other participants included Mr. Lewis Bevis, Miss Mary Wernersbach, Mr. Robert Gustus, Mr. Al Reinhardt, Mrs. Anna D. Thiel, Miss Mary Hester and Miss Charlotte Meade.

Also included on the program was a discussion on "The Administrator Evaluates the Pharmacist," by Mr. D. O. McCluskey, administrator at Druid City Hospital, Tuscaloosa, Ala.

Members of the Florida Society were welcomed by Mr. Tracy Hare, president of the Florida Hospital Association.

Massachusetts Society

Dr. T. C. Fleming of Hoffmann-La Roche was the principal speaker at the November 18 dinner meeting of the Massachusetts Society. He discussed "Drugs Affecting the Vascular System," presenting an entertaining as well as informative talk. Guests for the meeting included members of the Connecticut and Rhode Island Societies and Miss Gloria Niemeyer, Secretary of the ASHP.

During the business meeting, an open discussion was held giving members an opportunity to raise questions concerning relationship with the national organization and plans for the annual meeting which is to be held in Boston in August.

Mississippi Society

The Mississippi Society of Hospital Pharmacists has applied for affiliation with the national organization. Officers of the group are President Sister Mary Carl, St. Dominics Hospital, Jackson; Vice-President Mr. James T. Brookshier, V. A. Hospital, Jackson; Secretary Mrs. Inez Cameron, St. Dominics Hospital, Jackson; and Treasurer, Mr. Lee Cameron, V. A. Hospital, Jackson.

Oklahoma Society

Members of the Oklahoma Society of Hospital Pharmacists met at the College of Pharmacy in Norman for an all-day meeting on November 14. Dean Ralph W. Clark and other members of the faculty at the College participated in the program and Mr. E. R. Weaver, secretary of the Oklahoma State Pharmaceutical Association, brought greetings. Professor Jean Brown discussed hospital pharmacy in general, emphasizing the unlimited opportunities for pharmacists in hospitals to give professional service. She pointed out the importance for pharmacists interested in this specialty to take training under the supervision of an experienced hospital pharmacist.

Following the presentation of papers, those attending the meeting toured the manufacturing laboratory of the School.

At a business meeting held at St. Anthony Hospital in Oklahoma City on December 16, plans were outlined for future meetings of the Oklahoma Society. The business session was followed by a Christmas party.

Philadelphia Association

Dr. E. J. Foley, Director of Medical Service, Winthrop-Stearns, Inc., was the principal speaker at the December 16 meeting of the Philadelphia Hospital Pharmacists' Association. He discussed two drugs—Levophed and Alevaire—covering uses, indications and cautions.

The meeting was held at the Holland Restaurant in Philadelphia with the dinner sponsored by Winthrop-Stearns.

Northeastern New York Society

Members of the Northeastern New York Society of Hospital Pharmacists are planning a visit to Lederle Laboratories sometime in February The December meeting of the group was in the form of a

Christmas party held at Leonard Hospital in Troy, N. Y. with Miss Lucy Manvel, Chief Pharmacist, as hostess.

Northern California Society

Mr. Claude L. Busick, Chief Pharmacist at St. Joseph's Hospital in Stockton, California, has been elected president of the Northern California Society of Hospital Pharmacists. Other new officers for 1954 include Vice-President Mr. Alphonse A. Seubert, Senior Pharmacist at the University of California Hospital in San Francisco; Secretary Mrs. Marie B. Kuck, Chief Pharmacist at St. Luke's Hospital, San Francisco; and Treasurer Mr. Stanley Marincik, Chief Pharmacist at the University of California Hospital in San Francisco.

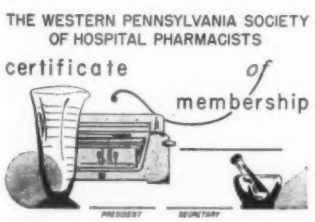
The December 8 meeting of the Northern California Society was held at St. Luke's Hospital in San Francisco with Dr. John J. Bertrand, Director of Medical Physics at St. Mary's Hospital, as speaker. He discussed the use of radioactive drugs in medicine.

Plans are being made by the Northern California Society to hold a two-day Institute in July. It will be sponsored by the Association of Western Hospitals and other affiliated chapters in the West will participate.

The project of the group for the current year will be a study of the possibility of compiling a "National Formulary for Hospitals." This would be designed to either eliminate the individual hospital formulary or serve as a guide for writing and compiling a formulary for each individual hospital.

Western Pennsylvania Society

The certificate shown below was designed by Mr. Max Helfand, Past President of the Western Pennsylvania Society. All members of the local group receive the certificate.



Southern California

Members of the Southern California Society of Hospital Pharmacists met on November 11 at the Good Samaritan Hospital in Los Angeles. Included on the program was a film on Varidase provided by Lederle Laboratories.

New officers were installed at the January 13 meeting of the Southern California Society held at Queen of Angels Hospital. Those who will serve during 1954 include President Lillie Wiel; Vice-President Joseph Ball; Recording Secretary Nelly Nigro; and Treasurer James Robinson.

The program for the January 13 meeting included a panel discussion entitled "Medical Team Work in the Hospital" with Mr. Walter Hitzelberger acting as moderator. Panel members were Edward Koziol, M. D., presenting the viewpoint of the physician; Mrs. Kathleen O'Flynn, R.N., presenting the viewpoint of the nurse; and Joseph Ball, pharmacist.

Toledo Society

Clarence Buell, Chief Pharmacist at Toledo Hospital, was installed as president of the Toledo Society of Hospital Pharmacists at the January 12 meeting. Other new officers are Vice-President Sister Mary John, Chief Pharmacist at Mercy Hospital, Toledo; and Secretary-Treasurer Eula Smith, Chief Pharmacist at Flower Hospital, Toledo. New members of the Society are Eric Theller of Fremont Memorial Hospital, and Alice Banachowski, Riverside Hospital.

Plans were made to hold a dinner meeting at Toledo Hospital on February 16.

Indiana Chapter

The fourth quarterly meeting of the Indiana Chapter of the ASHP was held at Veterans Hospital in Fort Wayne on November 14 and 15. During the business Allen Beck reported on the annual meeting and Miss Rhea Thomas reported on the British Pharmaceutical Conference which was held in London in August and on the meeting of the International Pharmaceutical Federation held in Paris in September. Plans for the 1954 Institute on Hospital Pharmacy were outlined and specific suggestions for papers were made by the individual members.

The afternoon session included a tour of the new Parkview Memorial Hospital.

The Indiana Chapter has inaugurated a page devoted to hospital pharmacy in the **Indiana Pharmacist,** official publication of the Indiana Pharmaceutical Association.

Midwest Sister Pharmacists

Members of the Midwest Association of Sister Pharmacists held a recent meeting at Baxter Laboratories in Morton Grove, Ill. After a tour of the plant where parenteral solutions are made, the regular business meeting was held.

Current projects of the Midwest Association include finding a suitable varnish for labels and a study of solutions for sterilizing thermometers. Results of the Pricing Project which is now completed will be referred to the national Committee on Special Projects..

Arizona Society

The Arizona Society is proceeding with a project to study the various forms used in hospital pharmacies throughout the United States. A request has been made asking all hospital pharmacists to forward three sets of the forms used in his hospital to: Miss Frances McKinney, Secretary, Arizona Society of Hospital Pharmacists, 338 E. Portland, Phoenix, Ariz.

Members of the Arizona Society met at Saint Mary's Hospital in Tucson on November 15. Mrs. Myrdas Brewer reported on the annual meeting of the ASHP which was held in Salt Lake City in August.

Texas Society

The Texas Society of Hospital Pharmacists will meet on Saturday and Sunday, March 20 and 21 at the University of Texas, Austin. Meetings will be held in conjunction with the Sixth Annual Hospital Pharmacy Seminar in Texas.

Maryland Society

Members of the Maryland Society met at the Clinical Center of the National Institutes of Health on December 8. Following the business session, the group toured the pharmacy department where Mr. Milton Skolaut is chief pharmacist.

Future meetings of the Maryland Society are scheduled for January 16 at The John Hopkins Hospital in Baltimore and for March 13 at Church Home Hospital, Baltimore.

as the president sees it

ALLEN V. R. BECK
Indiana University Medical Center, Indianapolis, Ind.

First, I would like to thank all of the affiliated chapter secretaries for their notices of meeting dates. This fine response means that all of you are interested in SOCIETY affairs. In the near future I will be traveling around the country visiting with many of you in meetings, and do not be surprised if I just come to visit you in your pharmacies. A closely knit organization can always progress.

The second meeting of the Joint Committee of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS and the American Hospital Association is scheduled for Chicago in the near future. The first meeting was somewhat of an exploratory one to acquaint all members with the objectives of said Committee. Progress was made, and we are all looking forward to the forthcoming meeting in anticipation of starting discussions which should benefit hospitals and hospital pharmacy in the United States.

While attending the A.A.A.S. convention in Boston, I had a chance to talk to some members of the Connecticut Society and the Massachusetts Society. Plans are underway for the annual Institute to be held in Storrs, Conn., in June and the Planning Committee will meet in Chicago very soon. This is an institute for you. We, the Planning Committee, can only arrange a program which includes the subjects we feel are of greatest interest. As with all SOCIETY activities, we want to provide a program which meets your needs. Should any of you have suggestions for speakers or topics for the Institute program, please contact me or any member of your Planning Committee. We are looking forward to an outstanding program and a student body larger than ever before. Each of you who has not attended an institute in the past should make plans now to be in Connecticut during the week of June 28, 1954.

I spent three days in New York working with Bob Bogash on the Institute program, as well as an outline for the Annual Meeting. These programs take much time to arrange. Should any of you have papers that might be presented, please contact Mr. Bogash. The ASHP Annual Meeting will be held in conjunction with the A.Ph.A. Convention in Boston during the week of August 22.

February 4 is the date set for the Interprofessional Conference sponsored by the American Pharmaceutical Association. The meetings will be held in Washington and your SOCIETY will be represented by George Archambault, Don E. Francke, Walter Frazier, J. Solon Mordell, Gloria Niemeyer, W. Arthur Purdum, and Vernon O. Trygstad along with your president. This meeting is being called as the result of action taken at the 1953 Convention and it is hoped that the discussions will serve as a basis for developing an interprofessional code of ethics. Representatives of the health professions as well as all phases of pharmacy have been invited to participate in the Conference.

EXECUTIVE COMMITTEE TO MEET

The ASHP Executive Committee will meet in Washington on February 26 and 27. Since this body meets but once a year, it is necessary to consider many matters of importance to the future of the SOCIETY. In addition to routine work, the Committee will give consideration to some long-range plans and special projects which will be of interest to all hospital pharmacists. Two new chapters of the ASHP will be considered for affiliation and attention will be given to the work being done in the local groups.

Your SOCIETY affairs are progressing and we hope to lend our assistance to committees, conferences, or meetings in any way possible for the betterment of hospital pharmacy.

Allen V. R. Beck

NEWS

Trygstad Appointed Director VA Pharmacy Service

V. O. Trygstad

Mr. Vernon O. Trygstad has been appointed director of the Veterans Administration Pharmacy Service, succeeding Mr. E. Burns Geiger who has served in this capacity for the past six years. Mr. Geiger, who assisted in the organization and supervision of VA's present pharmacy program, has played an important role in providing pharmacy services in the VA hospitals throughout the nation. He leaves the Veterans Administration to become affiliated with J. B. Roerig and Company, Chicago, Ill.

Mr. Trygstad, who has been Assistant Chief of the Pharmacy Division since 1951, has also played an active role in hospital pharmacy. His work as chairman of the Special Committee on Narcotic Regulations is well-known to ASHP members. He attended Hamline University and North Dakota State College, receiving his B. S. degree in pharmacy in 1936. He practiced retail pharmacy until 1940 when he was appointed a narcotic agent in the Federal Bureau of Narcotics, assigned to duty in New York City and later in Washington, D.C. He later served on active duty with the U.S. Navy and was first employed with the Veterans Administration as Chief of the Pharmacy Section of the former VA Branch Office in St. Paul, Minn.

Bowles Accepts New Position

Grover C. Bowles, immediate past-president of the Society, has been appointed to the central staff of Associate Hospital Administrators of the Memorial Hospital Association of Kentucky, Inc. He is presently serving as a consultant and will be with the Association on a full-time basis early in the spring. Under the direction of Mr. Gordon A. Friesen, Senior Hospital Administrator, Mr. Bowles will be responsible for paramedical services, including primarily pharmacy, manufacturing and dispensing, and central sterile supply.

The Memorial Hospital Association of Kentucky, Inc., provides for a coordinated hospital system under the United Mine Workers of America Welfare and Retirement Fund. Ten hospitals located in Kentucky, West Virginia and Virginia will be constructed with a central service plant. Location of hospitals in Kentucky will be at Harlan, Hazard, Whitesburg, Pikeville, McDowell and Middlesboro; in Virginia at Wise; and in West Virginia at Williamson, Man and Beckley. The total plan is an effort toward coordination of hospital services and standardizing methods, materials and maintenance. Included in the group operation will be a service center pharmacy where drugs will be compounded for the entire hospital system, comprising more than 1,000 beds. Mr. Bowles, as administrator of the paramedical services will be in charge of the central pharmacy and pharmacists will be employed at each of the other hospitals.

Mr. Bowles has been active in the ASHP and the A.Ph.A. for a number of years. Since graduation from the College of Pharmacy of the University of Tennessee in 1942, he has spent time at the Bowman Gray School of Medicine, University Hospital at University of Michigan, and the College of Pharmacy at University of Tennessee. Since 1949 he has been Chief Pharmacist at the Strong Memorial Hospital in Rochester, N. Y.

1954 Annual Meeting

The 1954 Annual Meeting of the American Society of Hospital Pharmacists will be held in conjunction with the A.Ph.A. Convention in Boston, Mass. during the week of August 22. Mr. Robert Bogash, Director of the Pharmacy Department at Lenox Hill Hospital, New York City, is chairman of the Program Committee. Papers for contribution to the program should be forwarded to him for review not later than May 15.

Definite arrangements for the time of meetings have not yet been set; however, local affiliated chapters will be notified and it is anticipated that every hospital pharmacy organization in the country will be represented.

Special arrangements are being made for tours of hospital pharmacies and other places of interest by the Massachusetts Society of Hospital Pharmacists.

G. F. Archambault

C. L. Busick

Sister Berenice

ASHP Officers for 1954-1955

George F. Archambault, Chief of the Pharmacy Branch of the Division of Hospitals, U.S. Public Health Service, Washington, D. C., has been elected president of the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS for the 1954-1955 term. Dr. Archambault is a charter member of the SOCIETY and is well known to the membership through his participation in the Institutes and service on numerous committees. He is a graduate of the Massachusetts College of Pharmacy and holds an LL.B. degree from the Northeastern University's Schools of Business and Law.

The vice-president-elect, Mr. Claude Busick, is chief pharmacist at St. Joseph's Hospital in Stockton, California. He has played an active role in hospital pharmacy organizations on both the local and national level. During the current year, Mr. Busick is serving as president of the Northern California Society of Hospital Pharmacists.

Sister Mary Berenice, the treasurer-elect, is chief pharmacist at St. Mary's Hospital in St. Louis, Missouri. A charter member of the SOCIETY, Sister Berenice has participated in hospital pharmacy activities for many years. In addition to taking an active part in the Hospital Pharmacists' Association of Greater St. Louis, she has served on national committees and last year was a member of the ASHP Executive Committee.

The ballots were counted by a committee of four ASHP members appointed by President Allen V. R. Beck and the results submitted to the Secretary, Gloria Niemeyer. Included on the Committee were Allen J. Brands, Bureau of Indian Affairs, Washington, D. C.; Mary Ann Coleman, Hospital for the Women of Maryland, Baltimore, Md.; Stephen W. Ruth, Church Home and Hospital, Baltimore, Md.; and John F. White, George Washington University Hospital, Washington, D. C.

Graduate Program Announced

Announcement has been made of a graduate program in hospital pharmacy at The University of Connecticut in combination with an internship at Hartford Hospital. The course of study at the University includes biochemistry, pharmacology, parenteral preparations, chemistry of organic medicinal products, manufacturing pharmacy, hospital pharmacy administration and seminar leading to a Master of Science degree by the University and a certificate of internship by the Hartford Hospital. The internship includes practical experience in hospital policy administration, pharmaceutical manufacturing, prescription compounding and dispensing, preparation of sterile solutions and other sterile products, and attendance at medical seminars held at the hospital.

Appointments are made for a twenty-three month period beginning July first of each year. During the academic year interns devote one-half time to graduate study. The applicant must be a registered pharmacist and a graduate of a college of pharmacy accredited by the American Council on Pharmaceutical Education. The applicant must be accepted by the Hartford Hospital and admitted to the Graduate School of the University of Connecticut. Applications for Graduate Study may be obtained from the Dean of the Graduate School, University of Connecticut, Storrs, Connecticut.

Woods Appointed Director of Extension Services

William E. Woods has been appointed director of the Division of Pharmacy Extension Services at the University of Texas. Mr. Woods is a graduate of the College of Pharmacy at University of Texas and recently received the LL.B. degree from the Law School. A native of Texas, he has had experience in retail pharmacy and served as a commissioned officer in the Public Health Service. He was later a member of the staff of The Pharmaceutical Survey. Mr. Woods is a member of the ASHP as well as the A.Ph.A.

Clarence Miller Appointed Assistant Director

Clarence Miller has been appointed Assistant Director at the Euclid-Glenville Hospital in Euclid, Ohio. Mr. Miller was formerly pharmacist there from 1946 to 1952, when he became personnel and purchasing officer. He earlier served a pharmacy internship at the University Hospitals in Cleveland, Ohio, where he subsequently was employed as a staff pharmacist. Mr. Miller is a member of the American Pharmaceutical Association and the AMERICAN SOCIETY OF HOSPITAL PHARMACISTS.

Appointees to Editorial Staff

Three hospital pharmacists have been appointed to the editorial staff of THE BULLETIN for 1954. The new Contributing Editors are Miss Joanne Branson, Mr. Paul Parker and Mr. Clifton Latiolais.

Miss Branson, a graduate of the School of Pharmacy, Western Reserve University, has served on the pharmacy staff of the Hospital Division of the Medical College of Virginia and later was Chief Pharmacist at Holy Family Hospital in Manitowoc, Wisconsin. At present she is Assistant-to-the-Chief Pharmacist at the University Hospital, Ann Arbor, Michigan.

Mr. Paul Parker, a graduate of the University of Michigan with B.S. and M.S. degrees, completed the internship at University Hospital in 1951. He served on the staff at University Hospital for two years during which time he also was on the editorial staff of THE BULLETIN. Mr. Parker is now Chief Pharmacist at the University of Chicago Clinics, Chicago, Illinois.

Mr. Clifton Latiolais, a native of Louisiana, received his undergraduate training in pharmacy from Loyola University College of Pharmacy in New Orleans and later completed the internship program in hospital pharmacy at University of Michigan, receiving a Master of Science degree. He is now Assistant Chief Pharmacist at the University of Chicago Clinics, Chicago, Ill.

Reprints Available

The following reprints which are of interest to hospital pharmacists are available from The Bulletin of the ASHP, 2215 Constitution Ave., N.W., Washington, D. C.:

Comprehensive Bibliography on Hospital Pharmacy, 1951—$1.00.

Supplement to Comprehensive Bibliography on Hospital Pharmacy, 1953—$1.00.

Ten Years of the American Society of Hospital Pharmacists—$1.50.

The Formulary System in Hospitals (Editorial) —no charge for single copies.

Sister Albertine Appointed Superior

Sister Mary Albertine, Pharmacist at Queen of Angels Hospital in Los Angeles, has been appointed Sister Superior of the Convent and Sisters at Queen of Angels. Sister Albertine has been active in the SOCIETY and the Southern California Chapter.

Clifton Latiolais

Joanne Branson

Paul Parker

Participants in the Tuesday afternoon Pharmacy Program of the American Association for the Advancement of Science, held in Boston, December 29, included, left to right: Dr. Charles U. Letourneau of the American Hospital Association; Mr. L. Parsons, Editor of The Apothecary; Dr. Kenneth Nelson of the Public Health Service; Dr. Dean Clark, Administrator of the Massachusetts General Hospital; Dr. Don E. Francke of the ASHP Bulletin; Dean Linwood Tice of the Philadelphia College of Pharmacy; President Allen V. R. Beck of the ASHP; Chief Pharmacist John Murphy of the Massachusetts General Hospital; and Dr. William E. Hassen, Jr. of the Peter Bent Brigham Hospital Pharmacy.

Pharmacists Meet with A.A.A.S. in Boston

A highly successful meeting of the Pharmacy Subsection of the American Association for the Advancement of Science was held in Boston, December 28 and 29, 1953. The program was arranged by Dr. George Archambault of the U. S. Public Health Service and was published in the September-October 1953 issue of THE BULLETIN.

All sections of the pharmaceutical profession were represented at this meeting and included participants from the fields of retail, manufacturing, hospital, teaching, wholesale pharmacy, and the pharmaceutical press. In addition, Dr. Dean Clark, Administrator of the Massachusetts General Hospital, and Dr. Charles U. Letourneau, Secretary of the Council on Professional Practice of the American Hospital Association, represented hospitals in the panel discussion on Accreditation of Hospitals: Its Effects on Pharmaceutical Service and Better Patient Care. Members of the Massachusetts, Connecticut, Rhode Island, and Delaware Societies were also active in the meeting.

Several of the outstanding papers presented at this meeting will be published in future issues of THE BULLETIN.

A.Ph.A. Election Results

Newly elected officers of the American Pharmaceutical Association who will be installed at the annual convention in Boston during the week of August 22 are: *President-Elect,* Newell Stewart, Phoenix, Ariz.; *First Vice-President-Elect,* John B. Heinz, Salt Lake City, Utah; and *Second Vice-President-Elect,* Ronald V. Robertson, Spokane, Washington.

Members-elect of the Council are George D. Beal, Pittsburgh, Pa.; Glenn L. Jenkins, Lafayette, Ind.; and Ernest Little, Newark, N. J.

Texas Seminar

President Allen V. R. Beck and Past President Grover C. Bowles will participate in the Sixth Annual Hospital Pharmacy Seminar being held March 20 and 21 at the University of Texas. Other participants will include outstanding pharmacists and clinicians who will discuss new trends in therapeutics, hospital pharmacy manufacturing, and other subjects of current interest to those practicing in this specialty. The annual seminar is sponsored by the College of Pharmacy and the Division of Extension of the University of Texas. A meeting of the Texas Society of Hospital Pharmacists will be held in conjunction with the two-day conference.

Career Brochure Available

"Shall I Study Pharmacy" is the name of a career brochure recently made available by the American Association of Colleges of Pharmacy. Intended to supplement college catalogs and for the guidance of counsellors, teachers and principals in high schools, the booklet serves a useful purpose. General information about the various specialties in pharmacy, a list of the accredited schools of pharmacy, legal requirements for practicing in the profession and sources of additional information make this a valuable booklet for the student who is interested in entering the profession.

Of special interest to hospital pharmacists is the following statement:

"A special field in pharmacy of rapidly growing promise and prominence is *hospital pharmacy.* Duties of the hospital pharmacists are very similar to those of the pharmacist who specializes in prescriptions. But hospital pharmacy also has certain features more likely to be found only in hospitals—preparation of "tailor-made" medicines, stocking of baskets of medicines for use by physicians and nurses, and administrative procedures peculiar to hospitals. To manage a large hospital pharmacy, long years of experience or a year or two of special study of hospital pharmacy are required. Hence, we find an increasing number of colleges of pharmacy offering postgraduate courses in this important field. These special courses in hospital pharmacy usually require two years of additional study, in which graduate course work is combined with internship in a hospital pharmacy."

Copies of the brochure are available at thirty-five cents each; three for one dollar; ten for three dollars; twenty for five dollars; and 100 or more at twenty dollars per hundred. Orders should be addressed to: R. A. Deno, Secretary, American Association of Colleges of Pharmacy, University of Michigan College of Pharmacy, Ann Arbor, Mich.

Radioactive Research Tools Available Free

A limited supply of radioactive corticosterone (Compound B) is now available to qualified investigators, free of charge, through funds supplied by the Public Health Service's National Institute of Arthritis and Metabolic Diseases. Availability of cortisone acetate and hydrocortisone acetate was announced by the National Institutes of Health on July 9, 1953.

Also available, obtained as intermediates in the synthesis of cortisone acetate, are:

Pregnane-3,11,20-trione

3α,17α-dihydroxypregnane,11,20-dione

17α,hydroxy-21-acetoxypregnane,3,11,20-trione.

In addition, microcurie samples are available of:

3α,17α-dihydroxy-21-acetoxypregnane,11,20-dione

3α,acetoxypregnane,11,20-dione.

These compounds are all labeled at position 4 with C^{14}, and have a specific activity of 0.49 mc./m.mole, except the corticosterone, which has a specific activity of 1.47 mc./m.mole.

Cortisone acetate, identically labeled, having a specific activity of approximately 1/3 that of the previously announced cortisone acetate may also be obtained.

Requests, in the form of a letter concisely describing the proposed research may be sent to the Endocrinology Study Section, Division of Research Grants, National Institutes of Health, Bethesda 14, Maryland. Transfer and use of these materials are subject to current Atomic Energy Commission regulations.

The preparation of these steroids was guided by a committee composed of Drs. T. F. Gallagher of the Sloan-Kettering Institute for Cancer Research, Gregory Pincus of The Worcester Foundation for Experimental Biology, and Max Tishler of Merck & Co., Inc. The Endocrinology Study Section of the National Institutes of Health, Dr. Charles B. Huggins, Chairman, and Dr. Sam R. Hall, Executive Secretary, have administered the program.

The United States Atomic Energy Commission gave the radiocarbon. Charles E. Frosst and Company synthesized the radiocortisone with help donated by The Upjohn Company. Tracerlab, Inc., supplied the methyl iodide. The Worcester Foundation, utilizing progesterone prepared by Frosst, bio-synthesized the corticosterone.

POLYSAL*

The Balanced Electrolyte Solution

IS PHARMACOLOGICAL

Here's why

POLYSAL prevents and corrects hypopotassemia without danger of toxicity.

POLYSAL corrects moderate acidosis without inducing alkalosis.

POLYSAL replaces the electrolytes in extracellular fluid.

POLYSAL induces copious excretion of urine and salt.

● Polysal, a *single* solution to build electrolyte and fluid balance, is recommended for electrolyte and fluid replacement in all medical, surgical and pediatric patients where saline or other electrolyte solutions would ordinarily be given. Now available in two convenient forms: Polysal in distilled water (250 cc. and 1000 cc.) and 5% Dextrose in Polysal (500 cc. and 1000 cc.).

*TM.

Stock POLYSAL Routinely

Clip for reference

COMPARISON OF PLASMA WITH REPLACEMENT SOLUTIONS

All concentrations in mEq (Milli-equivalents) per liter

Solution	Sodium (Na)	Chloride (Cl)	Bicarbonate (HCO_3)	Potassium (K)	Calcium (Ca)	Magnesium (Mg)
Plasma	140	103	27	5	5	3
POLYSAL**	140	103	55*	10	5	3
0.9% NaCl	154	154	0	0	0	0
M/6 Sodium Lactate	167	0	167‡	0	0	0
Ringer's USP	147	155.5	0	4	4.5	0
Hartmann's USP	130	109	28‡	4	3	0
Darrow's (KNL)**	122	104	53‡	35	0	0

* Obtained by metabolism of acetate 47 and citrate 8. ** Cutter Trademark.
‡ Obtained by the theoretical 100% metabolism of r-lactate

Stock POLYSAL ... A single solution to build electrolyte balance.

CUTTER Laboratories — CUTTER

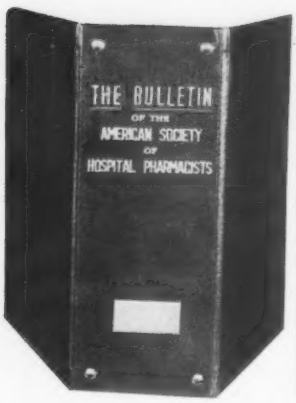
PERMANENT BINDER

FOR

The BULLETIN

of the

A.S.H.P.



$3.00 POSTPAID

4 or more $2.50 each

Purchase price refunded if not completely satisfied.

This new custom made binder is now large enough to contain the Decennial issue in addition to the new larger editions of THE BULLETIN. It is made of heavy ¼ inch cardboard, covered with waterproofed red leather reproduction, with the name die stamped in gold on the side with a special marking block provided to date the editions in the binder. It is manufacured to hold all the editions of THE BULLETIN issued during a two year period (12 issues). This binder has the approval of the publications committee of the A.S.H.P.

P. O. BOX 5544
BINDER-A.S.H.P.
FRIENDSHIP STATION
WASHINGTON 16, D.C.

I enclose $_____ for ____ binder(s) which you will send postpaid.

NAME_____

STREET_____

CITY_____ ZONE____

STATE_____

MEETING DATES - 1954 and 1955

Southeastern Society of Hospital Pharmacists—April 7-9, 1954, Atlanta, Ga.

New England Hospital Assembly—March 29-April 1, 1954, Boston, Mass.

Midwest Hospital Association—April 28-30, 1954, Kansas City, Mo.

Tri-State Hospital Assembly—May 3-5, Chicago Ill.

Catholic Hospital Association—May 17-20, 1954, Atlantic City, N. J.

Catholic Hospital Association Institute on Hospital Pharmacy—May 17-19, 1954, Atlantic City, N. J.

Middle Atlantic Hospital Assembly—May 26-28, 1954, Atlantic City, N. J.

A.H.A.-A.Ph.A.-ASHP Institute on Hospital Pharmacy—June 28-July 2, 1954, Storrs, Conn.

American Pharmaceutical Association—August 22-27, 1954, Boston, Mass.

American Society of Hospital Pharmacists—August 23-24, 1954, Boston, Mass.

American Hospital Association—September 13-16, 1954, Chicago, Ill.

Maryland-District of Columbia-Delaware Hospital Association—November 8-9, 1954, Washington, D. C.

Pan-American Congress of Pharmacy—December, 1954, Sao Paulo, Brazil.

American Association for the Advancement of Science—December, 1954, San Francisco, Calif.

International Pharmaceutical Federation—September, 1955, London, England.

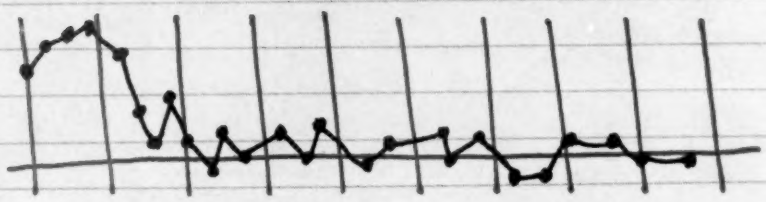
POLYETHYLENE TUBES FOR EYE SOLUTIONS

(Continued from page 42)

After the tubes are filled, they are capped with a leakproof cap which has also been sterilized. Gummed labels will not stick to polyethylene but may be fastened by wrapping them around the tube and overlapping the edges. Cellophane tape also may be used to secure the labels. The tubes are not re-used since we have found no practical method for cleaning them.

Polyethylene tubes are manufactured by Plax Corporation, Hartford, Connecticut. We find these tubes cost less than the eye solution bottles previously used. Tubes with closed ends are priced at $32.50 per 1,000 in quantities less than 2,000 pieces. Tubes with open ends are supplied at $27.50 per 1,000, but the ends must be closed by a special device which is quite expensive.

Dx/ Pneumonia



℞/ Terramycin®

brand of oxytetracycline

an antibiotic of choice

When the diagnosis is pneumonia, Terramycin therapy usually brings quick results because this broad-spectrum antibiotic is equally effective against coccal, Friedländer's and atypical virus pneumonia.

"After the administration of Terramycin, 59 of the [60] patients...improved rapidly with almost complete defervescence within twenty-four hours."[1]

Given in the recommended daily adult dose of 250 to 500 mg. q. 6 h., Terramycin is exceptionally well tolerated.

"There were no toxic manifestations from this antibiotic....No nausea or vomiting was noted. No patient developed leukopenia."[2]

Even cases that resisted previous treatment with other agents frequently show a gratifying response to Terramycin therapy.

"A case of staphylococcal pneumonia, complicated by tension pneumothorax which had shown no response to [another antibiotic], made a rapid, complete recovery on a dosage of 15 mg. per lb."[3]

1. Knight, V.: New York State J. Med. 50:2173 (Sept. 15) 1950.
2. Potterfield, T. G., and Starkweather, G. A.: J. Philadelphia Gen. Hosp. 2:6 (Jan.) 1951.
3. Swift, P. N.: Proc. Roy. Soc. Med. 44:1066 (Dec.) 1951.

Pfizer

PFIZER LABORATORIES
Division, Chas. Pfizer & Co., Inc.
Brooklyn 6, N. Y.

NEW MEMBERS

JANUARY 1, 1954

ARIZONA
Cook, Thomas D., 3435 W. Apache Rd., Phoenix

ARKANSAS
Brewer, Dayton, Lavaca

CALIFORNIA
Gutierrez, Eliseo, 440 S. Oxford, Los Angeles

DISTRICT OF COLUMBIA
McDonald, Ronald F., 616 Albee Bldg., Washington (A)

FLORIDA
Neidlinger, Lee M., 314 Manor Pl., Coral Gables

ILLINOIS
Allaben, James W., 1027 Haskell Ave., Rockford
Vrchota, 1st Lt. C. F., MSC, 6165 N. Ozark Ave.,Chicago

INDIANA
McCurdy, Marian E., Marion General Hospital, Marion

MARYLAND
Schaech, Dorothy F., 3024 Pinewood Ave., Baltimore

MASSACHUSETTS
Caron, Yolande T., 16 Dow St., Salem

MICHIGAN
DeMaria, Florine, Beal Residence, Ann Arbor (A)
Stevenson, Dale N., 1217 Willard, Ann Arbor (A)

NEW JERSEY
Callery, John V., 87 Grove Terrace, Irvington

NEW YORK
Craig, Preddis, 199 Northland Ave., Buffalo
Markunas, Walter M., Sunmount

NORTH CAROLINA
James, Cecil I., 819 Third St., Durham (A)

OHIO
Douglas, Hildah V., 1283 7th Ave., Akron
Novak, Evelyn J., St. Joseph Hospital, Lorain
Wu, Cynthia W. Y., 11501 Shaker Blvd., Cleveland (A)

PENNSYLVANIA
Caron, Norman R., 4312 Pine, Philadelphia (A)
Desiderio, Joseph A., 1138 Ritner St., Philadelphia
Desjardins, Joan A., 442 Gainsboro Rd., Drexel Hill
Kaplan, Anna N. B., 411 W. Girard Ave., Philadelphia
Phaff, Harry, 6224 Washington Ave., Philadelphia (A)

RHODE ISLAND
Gilberti, Edward L., 50 Graybar Rd., Warwick
Lang, William H., 69 Norman Ave., Pawtucket

TENNESSEE
Teague, Bascom R., 817 Shotwell St., Memphis

VIRGINIA
Marcus, Sidney R., 2413 N. Dehring St., Alexandria

WASHINGTON
Amabe, Emiko, 115 18th Ave., Seattle

Turn on the safety with Cytal*

The NEW, NON-HEMOLYTIC Irrigating Fluid

Cytal is safer

Urologists find Cytal safer—*because* it eliminates the danger of hemolysis . . . *because* it's produced under the same exacting standards as Cutter Saftiflask® I. V. Solutions . . . *because* it's non-irritating and free-flowing . . . *because* it's free of electrolytes and sticky sugars . . . *and because* this non-hemolytic fluid offers excellent optical qualities.

Cytal is convenient

Hospitals find Cytal convenient. A concentrated solution of hexitols and parabens, Cytal is ready for immediate use when diluted with 9 parts distilled water.

Cytal is economical

Hospitals also find Cytal economical. Considering the time and expense needed to prepare *other types* of non-hemolytic irrigating fluids, Cytal spells ECONOMY as well as SAFETY and CONVENIENCE.

*TM. Concentrated Cytal is available in 1 liter Saftiflasks. Sterile and pyrogen-free.